KCMC Clinical Trials Unit	STANDARD OPERATING PROCEDURE	Effective Date	SOP-Number CTU 002-02
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Title: SOURCE DOCUMENTATION

SOP References: Informed Consent Process, Study Visits, Managing Study Medications, Managing Toxicities, AE & SAE Reporting **Supersedes: N/A**

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PURPOSE: Documentation of source data is necessary for the reconstruction, evaluation, and validation of clinical findings, observations, and other activities during a clinical trial. Source documentation serves to substantiate the integrity of trial data, confirm observations that are recorded, and confirm the existence of subjects. This SOP also serves to ensure data quality by creating audit trails and enabling verification that data are present, complete, and accurate. Each specific research task lists the requirements that act assure quality data. These requirements are applicable to all research trials funded by the United States of America government and its Departments and/or Institutions.

Common requirements for all research tasks source documentation are:

- All data must be verifiable and all documentation needs an audit trail.
- Always refer to local, state, institution, institutional review board (IRB)/independent ethics committee (IEC) policies and procedures and follow them if they are more stringent.
- To achieve data quality, all data must be:.
    1. Attributable - Is it obvious who wrote it?
    2. Legible - Can it be read?
    3. Contemporaneous - Is the information current and in the correct time frame?
    4. Original - Is it a copy? Has it been altered?
    5. Accurate - Are conflicting data recorded elsewhere?

POLICY: This SOP has been adapted for the Kilimanjaro Christian Medical Centre (KCMC) Clinical Trials Unit (CTU) directly from the Division of AIDS Clinical Trials Group SOP Guidelines. 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, and 3) standards for good clinical practice (GCP).

RESPONSIBILITY: The Principal Investigator and all research personnel are responsible for following source documentation guidelines as outlined in this policy.

ADDENDA

Definition: Any addition or change to completed (signed and dated) research notes

Requirements:

- If source documentation is incorrect, incomplete, or otherwise deficient, it may be corrected/completed by making an additional entry or addendum to the source documentation. The later entry must be signed/initialed and dated.
- All addenda must be signed and dated in present time by the person making the entry.
- Sites must NOT modify past-dated source documentation in research records in an attempt to resolve deficiencies. Altering past-dated records is potentially fraudulent.

ASSENT

Definition: Permission or agreement by legally capable persos(s)

Requirements:

- Assent of children and permission of parents or legal guardians is required as determined by the IRB/IEC and local laws.
- State/local law where the research is taking place defines the age of a minor and requirements for emancipation.
- Local IRB/IEC determine the age for obtaining assent.
- The requirement for assent of children and/or permission of their parents or legal guardians may be waived by the IRB/IEC as long as the criteria for waiving consent in the regulations (45CFR46.408c) are met.
- Keep on file all versions submitted and approved by site's IRB/IEC.

CASE REPORT FORMS (CRF) USED AS SOURCE DOCUMENTATION

Requirements:

- Case report forms (CRFs) may be used as source documents if they represent data collected for the study and are where data were initially recorded.
  1. If data are obtained at a later date (i.e., after the study visit) and are recorded on the CRF as source documentation, it must be signed/initialed and dated.
  2. If data are transcribed from another source onto the CRF, the CRF is not considered to be the original source document and it cannot be used as source documentation. Examples of data that are routinely transcribed from other sources include: laboratory results, radiology reports, histories documented in referral letters, etc.
- CRFs used as source documents are not meant to replace ALL source documentation—there will still be a need for progress notes, lab results, X-rays, etc.
- CRFs used as source documentation need to be maintained and made available for review in the same manner as other source documents.

CHART NOTES

Requirements:

- Refers to all notes related to study visits that are entered in the research or medical record by site staff. (e.g., progress note, nursing note, clinic note, etc.)
  1. This does NOT apply to source documents that originate outside the site since the individuals making the notations may not be involved with the study.
  2. Follow the institution's record-keeping procedures if they are more stringent.
- All data entries must be signed/initialed and dated:
  1. Each time a new entry is made.
  2. By the person making the entry.
  3. Entries by different people must be signed/initialed and dated by the individual making the entry.

  Exceptions:

  Multiple entries to a source document made by the same person on the same day require only one signature/initials and date on the page IF there have been no interim entries made by other individuals. It is incumbent upon the individual signing the source document to ensure that there have been no entries other than his/her own.

  A single date on a document with multiple entries is permitted if all entries were made on that same date.

COMMUNICATIONS: VERBAL

Requirements:

- Verbal communications pertinent to research data collection must be documented in the research record in enough detail to support the data collected.
- Document in one of the following:
  1. Chart note
  2. Contact report (i.e., any written documentation of conversation that is signed and dated)

COMMUNICATIONS: WRITTEN

Requirements:

- Written communications pertinent to research data collection must be doc
- Documents must have appropriate identifiers to verify that they correspond to the specified subject.
- Includes documents such as the following examples:
  1. Letter
  2. Memo
  3. E-mail
  4. Reply correspondence
  5. Admission/discharge summaries

COMPLIANCE: STUDY DRUG/AGENT

	Compliance data is to be captured as specified by the protocol. • Document in one of the following: 1. Chart note 2. CRF used as source document 3. Pharmacy records To meet GCP Guidelines for documentation of compliance data, it is important to remember that compliance data has two components, quantitative data and qualitative data. • Quantitative data that should be captured includes: 1. Quantity of study drug/agent dispensed 2. Quantity returned, if any* 3. Reported number of missed doses *If the study does not provide the drugs/agents through the site or site pharmacy, but rather the subject secures drugs/agents through prescriptions filled at their own pharmacy, the information on quantity returned is not applicable. • Qualitative data that should be documented in a chart note include: 1. The directions for taking all study drugs/agents have been reviewed with the participant. 2. When study drugs/agents are initially provided. • At intervals determined by the protocol. 3. Deviations from the instructions or problems in following the instructions.

COMPUTER RECORDS (COMPUTERIZED SYSTEMS/ELECTRONIC RECORDS)

Requirements:	• When data are entered directly into a computer system, the electronic data in the computer system is the original source document. • A paper record (printout/hard copy/"print screen") of the electronic data is considered to be a copy. • Requirements for documentation, record keeping and record retention apply to computer records as they do for paper systems. • Computer records may be signed with an electronic signature. • One type of an electronic signature is when a user signs-on to a computer system using two (2) distinct identification components, such as an identification code (user name) AND a password. 1. Each electronic signature shall be unique to one individual and shall not be reused by, or reassigned to, anyone else. 2. Signed electronic records must contain information associated with the signing that clearly indicates all of the following: Printed name of the signer. Date and time when the signature was executed.

CONCOMITANT MEDICATION(S): NON-STUDY

Requirements:	• Document subject/caregiver reported use of concomitant medication, non-study drugs, and prohibited medication according to protocol requirements.

CONFIDENTIIALITY

Requirements:

Inform Subject

- Subjects must be informed of the extent to which confidentiality of records identifying them will be maintained:
  1. Extent permitted by law.
  2. Personal information is not released without subjects' written permission.
  3. Subjects are not personally identified in any publication about the study.
  4. Data is to be identified by code (e.g., PID) outside of the site.
  5. Research records may be reviewed by representatives of:

Research team personnel
Study monitors

Pharmaceutical companies involved in the study
Responsible IRB/IEC
Regulatory authority

A potential subject, in the informed consent process, must be made aware of the appropriate representatives that may review all of his/her medical records (research specific or otherwise) that are held by the institution conducting the research.

While the research-specific record is the document being monitored for compliance with regulations and guidelines, access to the full medical record held by the institution that is conducting the research must be available to monitors at the time of review for purposes of identifying supporting documentation of research record data.

Storage

- All research records must be securely stored:
  1. Double-lock when not in use.
  2. Restricted access during work hours and/or when unattended.
  3. Also refer to local institutional policies & procedures.

Labeling

All source documents must be labeled with subject identifiers to enable verification that the documents correspond to particular subjects.

Information Leaving the Site

If research records leave the site, follow local institution policy to ensure that confidentiality is maintained.

Contraception: protocol-required

Requirements	• Protocol required subject counseling on use of appropriate contraception must be documented prior to randomization/enrollment by one of the following: 1. Chart note with documentation to support the protocol defined entry criteria for contraception. 2. Completed Eligibility Checklist used as source documentation to support the protocol defined entry criteria for contraception. The Eligibility Checklist must correspond with the protocol text. • If the protocol specifies that the subject must agree to practice 1 (one) or more forms of contraception, document one of the following: 1. The methods the subject chooses to use. 2. Subject counseling which included all of the following information: The number of forms of contraception that are necessary; A list of acceptable forms of contraception was given to the subject; The subject agreed to use contraception when necessary. 3. Subject-reported history of menopause or sterilization (hysterectomy, oophorectomy, tubal ligation, or vasectomy). • Acceptable documentation to indicate that a child does not have reproductive potential: 1. Determine if onset of menses (in girls) or onset of puberty (in boys) has occurred: Subject/caregiver history Physical examination 2. If the subject is pre-pubescent: Document assessment and that the subject has not yet reached reproductive potential. Contraceptive counseling and pregnancy testing are not necessary. 3. If the subject has started menstruation—regardless of age—contraception counseling and pregnancy testing are required as specified by the protocol.

COPIES: CERTIFIED

Requirements:	• A copy-used as a source document should be certified that it was verified to be an exact copy of the original, having all of the same attributes and information as the original. 1. This provides an audit trail in the event that the copy appears to have been altered. • If the original document is retained elsewhere, the copy does NOT need to be certified (e.g., original lab results are filed in the laboratory). • Monitors and other authorized auditors may request to see the original documents or certified copies to verify validity of data for trial related monitoring. • Certification of a copy may be indicated by any of the following methods: 1. A signed/initialed and dated statement on the copy that indicates it is an exact copy of the original information. This is to be done by the person making the copy, or, the person verifying that the copy is the same as the original. The statement may be in the form of a stamp as long as it is accompanied by an original signature/initials and date. 2. Signature/initials and date without a statement. The dated signature/initials means that the signer has verified that the copy is an exact copy of the original. 3. Certification for copies received from an outside institution indicates it is an unaltered copy as received. • Documentation received via fax are NOT considered to be originals. • Printouts retrieved from an institution's computer system ARE copies if the electronic file is the original source document. • Documents consisting of more than one page may be verified in a package as being one (1) copy if the package of copies is to remain intact in the file. 1. For verification, the first page of the copy must have on it a signed and dated statement that indicates the package consisting of X (specify) number of pages is an exact copy of the original information. 2. Each page must then be initialed and dated to verify that it is part of the package.
DEATH	

Requirements:	• Document by one of the following: 1. Obituary 2. Autopsy report 3. Death certificate 4. Contact report documenting verbal communication with subject's healthcare provider, family member, significant other, friend, etc. • If the death is reported via verbal communication, the following must be recorded in the source document to substantiate the date reported cause of death: 1. Name of person reporting death and his/her relationship to subject 2. Date death reported to site 3. Date of death 4. Reported cause of death 5. Dates and methods site attempted to obtain official documentation to verify the verbal report of the date and cause of death • SAE reporting according to protocol, sponsor and institutional requirements.

DEPARTURES / DEVIATIONS / VIOLIATIONS

Requirements:	• All protocol departures/deviations/violations must be recorded in the subject's research record. • If pertinent, reasons for the departures and/or attempts to prevent or correct the departures are to be included in the documentation. • Refer to local IRB/IEC/institution policies for reporting protocol departures to the IRB/IEC. • Examples of departures. Include but are not limited to: 1. A missed visit needs a note stating it is a missed visit and the site's attempts to locate the subject to request that he/she come in to make up that visit. 2. Departures from protocol also include incomplete laboratory evaluations, physical assessments, questionnaires, etc. 3. Changes in procedures or medication based on clinical judgment need a note explaining the problem, what was done, communications with the protocol team and IRB/IEC if necessary, actions, and resolution. An AER may need to be filed.

DOCUMENTATIONS STANDARDS

	• All research personnel must comply with applicable standards for medical documentation as determined by their institutional policy, professional Code of Ethics, and licensing authority. • At a minimum, the following general standards must be followed: 1. Keep handwritten notes and signatures legible (if necessary, print name underneath the signature). 2. Sign and date all entries. Include credentials if required by the institution. 3. Make error corrections in the following manner: draw a single line through the incorrect information, initial, date, and state reason for change (if necessary). 4. Never obliterate entries that require correction. 5. Never destroy original documents if they require error correction. 6. Keep subject records secure yet accessible. 7. Do not alter past-dated notes, chart notes/progress notes (e.g., by writing alongside or adding to prior entries). 8. Only use dark ink. 9. Never use whiteout. 10. Never use pencils.
ENDPOINTS	
Requirements:	• For study defined clinical or laboratory-based endpoints, the subject's research record must document the specifics of the event(s) or test result(s) as required by the protocol. • Results of all diagnostic evaluations needed to substantiate the diagnosis must be included in the subject's research records. • Document endpoints by any of the following examples, as applicable to the type of endpoint (e.g., clinical or laboratory): 1. Chart note 2. Consult note 3. CRF used as a source document 4. Documentation of death 5. Radiology diagnostic interpretation 6. Laboratory report. 7. Paper copy of electronic report. 8. Hard/fax copy lab report from research/ commercial lab. 9. Hard/fax copy of correspondence from protocol team member (e.g., email from Data Manager) that subject has reached a study-defined lab based endpoint.

ENTRY CRITERIA (INCLUSION / EXCLUSION CRITERIA)

Requirements:	• Documentation to address each of the protocol's inclusion and exclusion criteria must be present in the research record. 1. Chart notes to address the entry criteria. 2. Eligibility checklists used as source documentation as long as the criteria included corresponds with the protocol and each inclusion/exclusion criterion is addressed. 3. Original documents or certified copies of protocol required diagnostic results and/or history (e.g., laboratory results, radiology report, medication history, etc.). • Documentation to address pertinent negatives must also be present in the research record. For example, exclusion criteria may require that the subject not be using any concomitant medications, or has not been diagnosed with any of a list of diseases. 1. Chart notes to address each negative criterion. For example, "None of the concomitant medications excluded by the protocol are being used by the subject" is an acceptable way to document that the criterion has been met. 2. Eligibility checklists used as source documentation as long as the criteria included corresponds with the protocol and each inclusion/exclusion criterion is addressed. 3. A blanket statement regarding <u>all</u> such exclusion criteria, such as "The subject does not meet any of the exclusion criteria outlined in the protocol" is NOT considered adequate.

ERROR CORRECTIONS

Requirements:	• Error corrections must be done as follows: 1. Draw a single line through the incorrect information. 2. Initial, date, and state reason for change (if necessary). 3. Insert the correction. • Never use pencil to write entries. • Never use "white-out". • Never obliterate entries that require correction. • Never destroy original documents, even if they require error correction. • Do not alter past-dated notes, chart notes/progress notes (e.g., by writing alongside or adding to prior entries). • Error corrections that are not done according to procedure will result in inadequate source documentation.

FLOW SHEETS

Requirements:	• Flow sheets to be used as source documentation must be: 1. Signed/initialed and dated by the clinician responsible for the entry. 2. Labeled with an appropriate subject identifier. • If more than one person makes entries on a flow sheet, each entry must be signed/initialed and dated. • Entries for timed serial evaluations (e.g., vital signs, pharmacokinetic studies, etc.) must also note times if required by the protocol.
IDENTIFIERS	
Requirements:	• All source documents must be consistently labeled with at least 1 (one) unique identifier so monitors can verify that documents correspond to particular subjects. • Examples of unique identifiers: 1. Hospital identification number 2. Medical record number 3. Social Security Number 4. Patient identification (PID) number 5. Full name if there are no other subjects with that name at the site 6. Two non-unique identifiers in combination • Identifiers that are NOT unique: 1. Date of birth 2. Subject initials 3. Full name if there are other subjects with that name at the site • Identifiers on original documents must NEVER be obliterated, even if a new identifier is added to the document (e.g., placing a PID label over a subject's name).

INFORMED CONSENT

Requirements:

- Informed consent must be documented by the use of a written consent form:

1. Except if the IRB/IEC has waived the requirement for a signed written consent form in accordance with the requirements of 45CFR46.117(c) and 21CFR56.109(c).

Documentation of the IRB's decision to waive the requirement for written consent must be present in the regulatory files at the site.

2. All consent forms must be approved by the local IRB/IEC.

3. All consent forms must be submitted to the sponsor for review.

4. All consent forms for new protocols and amendments must be approved by the sponsor, prior to submission to the IRB/IEC.

5. Protocol-specific consent must be obtained prior to randomizing/enrolling a subject.

- Signatures on the consent form:

1. Must be legal name and may not include fabricated/falsified names.

2. Must not use an initial for the last name.

3. Strongly recommend not using an initial for the first name; however, if the person commonly signs his/her name using an initial for the first name, it will be accepted as long as it is also acceptable as per the policy of the institution.

4. Must be in ink.

5. Must be dated by each person signing the form. It is NOT acceptable for research staff to complete the date for another signer.

- Federal regulations and institutional policy must be followed when screening subjects to determine potential eligibility.

1. Screening is defined as any procedure done solely for the purpose of determining a potential study subject's eligibility or to enter a subject into a research study.

2. Consent must be obtained before invasive procedures are performed.

3. It is required unless the IRB has waived the requirement for a signed written consent form as per the requirements of 21CFR56.109(c).

Documentation of the IRB's decision to waive the requirement for written consent must be present in the regulatory files at the site.

4. Either an IRB/IEC approved generic screening consent form or the IRB/IEC approved protocol consent form is acceptable.

5. If a site customarily uses IRB/IEC approved screening consents for all study subjects, or for all subjects screened for certain protocols:

The screening consent must be signed & dated before screening for protocol eligibility begins.

The protocol-specific consent must be signed & dated before randomization/enrollment into the protocol.

6. Access, and consent for access, to medical records and/or databases for use in identifying potentially eligible study subjects is dependant upon the policies of the local institution/IRB/IEC.

Review of medical records and/or databases outside of your institution is NOT permitted without the prior consent of the potential study subjects.

7. Maintain a list/log of subjects screened for a protocol.

- Information given to the subject or the representative must be in a language they can understand.

1. When the study subject population includes non-English speaking people so that the clinical investigator or the IRB/IEC anticipates that the consent interviews are likely to be conducted in a language other than English.

2. IRB/IEC approved translated consent form.

3. A consultant may be utilized to assure that the translation is correct.

4. A copy of the translated consent document must be given to each appropriate subject.

5. While a translator may be used to facilitate conversation with the subject, routine ad hoc translation of the consent document may NOT be substituted for a written translation.

6. If a non-English speaking subject is unexpectedly encountered, investigators will

INITIALS	
Requirements:	Initials may be used in place of signatures provided that a signature key inclusive of the following is maintained at the site or on the document itself: • Initials • Signature • Credentials (if applicable)
KARNOFSKY SCORE	
Requirements:	• Record in the research record the actual score assigned to a subject at a given point in time (as specified in the protocol). • Provide documentation as per protocol requirements.
LAB TESTS: SPECIMEN COLLECTION (RESEARCH AND ROUTINE)	
Requirements:	• Document that specimens were obtained as required by the protocol. • If required by the protocol, specimen collection time must be noted. • If fasting is required by the protocol, confirmation by subject of fasting more than 8 (eight) hours, or as specified by the protocol, must be noted. Some protocols may require that the specific date and time of the last food/fluids are recorded.
LAB TESTS: RESULTS (RESEARCH AND ROUTINE)	

Requirements:	• All reports must have appropriate subject identifiers and date of specimen collection. • Lab reports must identify where the test was performed. • When reporting lymphocyte counts/percentages, a notation of the corresponding CBC with differential to verify total lymphocyte count may be required, depending on the lab's reporting format. • For batched and/or blinded research lab analyses, no documentation of results is required in the subject's research record unless the unblinded results were disclosed to the site for the purposes of subject management, study termination, or re-randomization/step assignment.

MEDICAL HISTORY: GENERAL AND HIV-SPECIFIC

	• Written documentation of medical history as defined by protocol. Including, but not limited to, diagnoses, signs/symptoms, medications, tests. • Verbal history, recorded in research record, is acceptable. Note the source (person providing history). • Chart note or referring healthcare provider's letter is acceptable. • Obtain reports of laboratory tests, diagnostic procedures, and examinations as necessary to substantiate history.

Title: SOURCE DOCUMENTATION

SOP References: Informed Consent Process, Study Visits, Managing Study Medications, Managing Toxicities, AE & SAE Reporting **Supersedes: N/A**

MEDICAL RECORDS

Requirements:	• Review of medical records is necessary to extract all information that may be relevant to the protocol. 1. Monitors and regulatory auditors may request to see original documents or certified copies to verify validity of data for trial related monitoring. 2. The following are examples of data: physical exams, concomitant medications, signs and symptoms/adverse events, diagnoses, laboratory results, diagnostic reports, etc. • Medical records at institutions with primary care facilities: 1. All records including the subject's primary care chart must be accessible to the monitor for review/audits. 2. Note if records are missing and efforts to locate them. • Medical records from outside institutions and primary care providers: 1. Records sent from other treating facilities that are incorporated into the subject's research record. 2. Monitors and FDA auditors may request to see original documents or certified copies to verify validity of data for trial related monitoring. 3. Subject must sign a release form if needed. 4. Unique identifier. 5. Record in the research record efforts to obtain outside medical records as needed for protocol participation. 6. Notations of follow-up efforts for records requested but not received. • Monitors must have access to the source documents located in these records during audits.

PRESCRIPTIONS

Requirements:	• Prescriptions must include: 1. PID/SID numbers (subject's name instead if it is for a commercial pharmacy) 2. Name of study agent 3. Dose 4. Schedule 5. Route of administration, (or protocol number if that provides equivalent information) 6. Number of dosing units to be dispensed, OR, instructions (e.g., sufficient supply until next visit) in place of an exact quantity. • Prescriptions may be written with refills. Documentation of Changes in Study Treatment: • Any change in study drug/agent status must be documented with sufficient detail to support and provide an explanation for the change as recorded on the CRF. • Entries regarding dose modifications must include the reason for the change and the actual dosage change. • Notes regarding the holding of study drug/agent must include the reason for the hold. • Notes regarding the reinstitution of study drug/agent must include the reason for reinstitution of drug/agent and the dosage.

PROCEDURES: DIAGNOSTIC, THERAPEUTIC, SURGICAL, ETC.

Requirements:	As appropriate, results, interpretations and/or diagnostic procedures required by the protocol must be documented. For example: • Chart note • CRF used as a source document • Report • Flow sheet • Monitors and regulatory auditors may request to see the original document or certified copy to verify validity of data for trial related monitoring.

QUESTIONNAIRES: SUBJECT/GUARDIAN AND/OR STUDY PERSONNEL COMPLETED

Title: **SOURCE DOCUMENTATION**

SOP References: Informed Consent Process, Study Visits, Managing Study Medications, Managing Toxicities, AE & SAE Reporting **Supersedes: N/A**

Requirements:	• The actual data on a subject/guardian completed questionnaire or CRF does not need supporting source documentation. • Documentation is required is to show that the protocol required questionnaire was given to the subject/guardian in accordance with protocol requirements. 1. For example: Enter a note into the subject's chart indicating the questionnaire/form was given to the subject/guardian to complete on a specified date. Indicate on a checklist that the subject/guardian completed the specified form on a specified date. 2. If the questionnaire is NOT completed by the subject, indicate who completed it and why. 3. If questions are completed by study personnel: Those questions/sections must be signed/initialed and dated. Supporting documentation for data must be in the research record (when applicable). Note if the form was completed via study personnel interviewing the subject/guardian. This pertains ONLY to questions that are an actual part of the questionnaire/data, not information related to form keying or headers. 4. Retain copy of questionnaire, form, or test as per the protocol.

RESEARCH RECORD/FILE

Requirements:	• All documents that substantiate data collected and/or are relevant to a subject's participation in a clinical investigation constitute a research record. They include the following: 1. Subject-signed informed consent 2. Source documents 3. Case history 4. Investigational pharmacy records 5. CRFs • Individuals authorized to review the records may request to inspect any or all of the above types of documents. • Investigators are responsible for maintaining accurate and complete research records. • Each subject must consent in writing to direct access to his/her research record, including original medical records held by the institution conducting the research, for trial-related monitoring, audit, IRB review, and regulatory inspection by authorized individuals. • Sites must be able to produce a research record in its entirety for monitoring and/or audit. 1. Sites must provide direct access to each subject's research records, including the entire medical record held by the institution conducting the research. 2. Direct access to all records held at the institution is necessary for purposes of identifying and monitoring trial-related and/or pertinent data (e.g., medical history, contraindications for enrollment, adverse experiences, etc.) in the source documents. 3. The source of study data must be verifiable in original source documents or certified copies. • Shadow files are an adjunct to the subject's medical record or clinic chart. 1. These files, consisting of copied source documents, are intended to reflect a subject's complete, study specific record. 2. Copied documents in these files are NOT the original source documents. 3. Monitors and regulatory auditors may request to see the original documents or certified copies to verify validity of data for trial related monitoring. If the site is not able to produce original source documents or certified copies during a monitoring review, the data will be considered as having inadequate source documentation. 4. May include protocol required documentation such as the following examples: Informed consent Screening results Baseline events Vital status Clinical and laboratory findings Management of study drugs/agents and toxicities

SOURCE DOCUMENT

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Requirements:	• Any original documents or certified copies that include documentation pertaining to the subject's condition while on a research study. This includes but is not limited to the following: 1. Medical record 2. Clinic chart 3. CRFs used as source documents 4. Primary care provider's office chart 5. Laboratory reports and radiology reports 6. Flow sheets, medication records, prescriptions, EKG tracings, etc. • Upon request of the monitor, auditor, IRB/IEC, or regulatory authority, the investigator/institution must make available for direct access all requested documentation that may be relevant to the subject's trial participation. This includes CRFs and medical records. • If there is no supporting evidence to verify protocol-required data and procedures, source documentation will be considered inadequate.

STORAGE OF SOURCE DOCUMENTS

Requirements:	• Sites must retain research records according to Federal regulation, institutional policy, the protocol, and/or Group SOPs. Includes: 1. Source documents 2. CRFs 3. Pharmacy records 4. Regulatory files • For electronic data storage, the sponsor and regulatory officials expect to be able to reconstruct the study. 1. This applies not only to the data, but also how the data were obtained and managed. 2. All versions of application software, operating systems, and software development tools involved in processing of data or records need to be available as long as data or records associated with these versions are required to be retained. 3. Records should be backed up regularly in a way that would prevent a catastrophic loss and ensure the quality and integrity of the data. Backup records should be stored in a secure location specified in the SOPs. Storage needs to be separate from the original records, such as in a separate building or an off site facility. Backup and recovery logs need to be maintained to facilitate an assessment of the nature and scope of data loss resulting from a system failure.

STUDY DRUG/AGENT

Requirements:	• Supplied study drugs/agents are dispensed only upon the written order of the Investigator of Record (IoR) or upon the order of a licensed practitioner directly responsible to the IoR as stated on the Form FDA 1572 (IND studies) or authorized prescribers list (non-IND studies). • Study drug/agent use by the subject must be recorded in the research record. • Medications that meet one or more of the following criteria for protocol-specified drugs/agents or non-specified drugs/agents are considered to be "study drugs/agents": 1. Protocol-Specified Drugs/Agents Drugs/agents specified by name for use in the study. Risks for each of these drugs/agents must be included in the informed consent form. The protocol will specify whether SAE reporting is required and, if so, the intensity or level of AE reporting. 2. Non-Specified Drugs/Agents: In addition to any drugs/agents specifically named for use in a study, other drugs/agents that are being used to address the study's primary therapeutic objective(s) and any other study objective designated for this purpose by the protocol will be considered to be study drugs/agents. Includes drugs/agents that are not individually specified by name in the protocol nor distributed by the sponsor. Protocols may designate distinct types or classes of drugs/agents that will or will not be "study drugs/agents". Risks of individual non-specified drugs/agents do not need to be included in the informed consent document; however, general statements regarding study treatment risk may need to be made. For example, including common risks for relevant drug classes or referral to package inserts/approved patient education material need to be considered. The protocol will specify whether SAE reporting is required and, if so, the intensity or level of AE reporting. Unless the protocol gives further instructions, all drugs/agents meeting this definition must be taken into account in deciding the intensity of AE reporting and included in assessments concerning relationship of SAEs to "study drug/agent". 3. Some protocols may have BOTH "specified" and "non-specified" study drugs/agents.
STUDY DRUG/AGENT ACCOUNTABILITY	

Requirements:	• The Pharmacist of Record must keep records to account for the disposition of study drugs/agents by documenting the following: 1. Shipment records 2. Lot numbers • Allows tracking of: 1. Product lot numbers 2. Accountability • Documents that the study drugs/agents have been used according to the protocol. • Document the final accounting of study drugs/agents: 1. Received at the site 2. Dispensed to subjects 3. Returned by subjects 4. Returned to sponsor

TOXICITIES: GRADING (ADVERSE EVENTS, SIGNS AND SYMPTOMS, LAB RESULTS)

Requirements:	• All toxicities and/or signs/symptoms, including those reported by the subject, must be recorded in the subject's research record and graded: 1. An actual numerical grade that corresponds to the applicable toxicity table. 2. A written description that corresponds to the definitions in the applicable toxicity table. 3. Examples include: Chart Note Flow sheet Adverse Event (AE)/Symptom Checklist Annotated lab slip, signed and dated by responsible clinician Serious Adverse Event (SAE) form signed by clinician completing the form. 4. If toxicities and/or signs/symptoms are documented by non-study staff, the site staff must then document in the research record their assessment of the event, including grade and relationship to study drug/agent. For example, if a subject is seen in an emergency room for a stroke, the research clinician must document in the research record the grade and relationship of the event to the study drug/agent. • Reportable AEs/SAEs must have documentation to support the determination of relationship to study drug/agent when it is found to be "Not Related". (i.e., There must be an alternative, definitive etiology documented by the clinician.)

VITAL SIGNS AND OTHER ASSESSMENTS

Requirements:	• The protocol must specify the required vital signs (e.g., temperature, pulse, respirations, etc.) and other assessments (e.g., height, weight, body surface area, head circumference, etc.) and at which study visits they are required. • Record on one of the following: 1. Chart Note 2. Flow sheet 3. CRF used as source documentation

This SOP has been read and understood by:

Name	Date
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