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Document Title: **SCORE Manual: Appendix Source Documents Requirements**

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## SOURCE DOCUMENTS

Source documents must follow the requirements detailed in the [Source Documentation](#) section of the DAIDS SCORE Manual. The examples below describe acceptable clinical trial source documents.

### CASE REPORT FORMS USED AS SOURCE DOCUMENTS

Case report forms (CRFs) may be used as source documents if data will be initially recorded on the form and the intended use is prospectively stated in the protocol; however, it should not be general practice for all data collected during a clinical trial.

Clear documentation of which CRFs are being used as source documents should be readily available at the beginning of all monitoring visits. CRFs used as source documents must also be maintained and available for review in the same manner as other source documents.

Original CRFs used as source documents must be signed/initialed and dated (handwritten/or electronically, as applicable) by the individual recording the data to ensure a clear audit trail of who completed the document.

**Note:** Using CRFs as source documents (direct and real-time entry) is different than using printed copies of electronic or paper CRFs as source documents, and then transcribing the data into the CRFs.

If the CRS uses copies of CRFs (paper or electronic) as source documents, such as a worksheet or template, and will then transcribe this data into the study CRF, the CRS can identify these CRFs to be used as source document worksheets or templates in the CRS procedures.

Clear documentation of which CRFs are being used as source documents should be readily available at the beginning of all monitoring visits. CRFs used as source documents must also be maintained and available for review in the same manner as other source documents.

### Common Deficiencies

- Inadequately identifying who corrected a document and when it was corrected (missing signature/initials, date), and failing to provide supporting notes to justify the change
- Missing standard of care elements due to staff only focusing on study-specific CRF data/requirements
- Study CRF being used as source document but not identified in the protocol to be used as such
- Not following Good Documentation Practices (GDP) when making corrections (i.e., obliterating data, using pencil instead of pen)

## CHART NOTES/CONSULT NOTES

All notes entered in hospital records, clinical charts, or research charts (e.g., progress notes, nursing notes, clinic notes, etc.) are considered source documents, even if they are not generated by clinical research site staff. Because these notes provide information related to the participant's medical history, protocol compliance, outpatient/in-patient visits, etc., they may be related to an adverse event (AE), study endpoint, and/or other aspects of the protocol.

Institution staff (i.e., not part of the research team) may not be required to generate notes that adhere to attributable, legible, contemporaneous, original, accurate, and complete (ALCOA-C) principles and International Council for Harmonisation (ICH) Good Clinical Practices (GCP), hereinafter referred to as ICH E6.

#### Common Deficiencies

- Missing participant identifiers (e.g., notes that exclude a participant's last name) may prevent attribution of the source document to the applicable participant
- Not following all Attributable, Legible, Contemporaneous, Original, Accurate, and Complete (ALCOA-C) principles (e.g., lacking date, signature/initials)

#### COMMUNICATIONS: VERBAL

All verbal communications related to research data collection must be documented in detail to support the data collected. CRS staff must document the "who, what, and when" of any communication to gather data, along with supporting details. CRS staff may communicate with a third party, such as a participant's emergency contact, to obtain participant data (e.g., participant vital status) for documentation.

Signed and dated documentation that details actual or attempted communication with any of the following entities must be captured in the research record, contact report, or other source document:

- Participants
- Parent/legally authorized representative (LAR)
- Family members/significant others/emergency contacts
- Friends
- Healthcare providers
- Other healthcare facilities

#### Common Deficiency

- Omitting mandatory details when updating records, such as date and individual who contacted the participant (or participant's authorized third -party representative)

#### COMMUNICATIONS: WRITTEN

When collecting research data, a CRS staff's actual or attempted written communication must contain:

- Author and date of the communication
- Recipient of the communication
- Details to support the data provided
- Appropriate participant identifiers corresponding to a specific participant

Forms of written communication may include documents such as admission/discharge summaries, letters, memoranda, and email correspondence.

### Common Deficiency

- Omitting mandatory details when updating records, such as date and individual who contacted the participant (or participant's authorized third-party representative)

### **ELECTRONIC RECORDS (COMPUTERIZED SYSTEMS)**

When CRS staff enter data into a computerized system (e.g., computer, smartphone, electronic patient diary), the system's electronic record (and associated signature) is the original source document. These systems must comply with 21 Code of Federal Regulations (CFR) Part 11 and any applicable in-country regulatory requirements. Please refer to the DAIDS policy, [Electronic Information Systems](#), for additional information and requirements on the use of electronic records.

Electronic records include electronic medical records (EMRs)/electronic health records (EHRs), eDiaries, Microsoft (MS) Word/Excel documents, databases, electronic CRFs, electronic study product inventory and accountability records, electronic radiology computerized tomography scan or cardiology (electrocardiogram [EKG]) images and reports, text messages, emails, and electronic questionnaires.

CRS staff may use systems/software (e.g., email, MS Word/Excel) that lack the user access control, adequate audit trail, and/or regular backup schedule required to maintain reliable data. In this case, the individual electronically generating the data must print, sign and date the record. This paper copy is considered the source document and must not be discarded/replaced by a new printed, signed, and dated document.

When an institution cannot provide read-only system access for monitors/auditors/inspectors, site staff must log into the system to show any requested data in their presence.

### Common Deficiencies

- Computer system used to record clinical research data (source document) does not meet the requirements necessary to ensure data quality and integrity.
- EMR/EHR lacks privacy and security controls that allow regulatory inspectors to verify data quality and integrity during a regulatory inspection.
- CRS staff share user identifications (IDs)/passwords with others (e.g., staff members, monitors), attributing entries to the wrong user. Note: User IDs/passwords must never be shared.

### **CERTIFIED COPIES**

According to ICH E6 (1.63), a certified copy is: "A copy (irrespective of the type of media used) of the original record that has been verified (i.e., by a dated signature or by generation through a validated process) to have the same information, including data that describe the context, content, and structure, as the original." If original documents are retained elsewhere at a CRS, copies do not need to be certified (e.g., original laboratory results are filed in the laboratory). Certified copies may be required in instances such as:

- A copy of an EKG tracing printed on thermal paper that fades over time requires a certified copy to

ensure data are available through the required retention period.

- Copies of a participant medical chart from an external institution to support participant eligibility and/or an AE require a certified copy to be the CRS's source document, as the external institution's medical chart cannot be retained at the CRS.

CRS staff may create certified copies using any of the following methods:

- Adding a signed/initialed and dated statement on the copy that indicates it is an exact duplicate of the original information
  - This must be performed by the individual making the copy or the individual verifying that the copy is the same as the original.
  - Statements may be stamped if they include an original signature/initials and date.
- Adding a signature/initials and date without a statement
  - The dated signature/initials must reflect that the signatory has verified the document is an exact copy of the original per the CRS's standard operating procedures (SOPs) for creating certified copies.
  - Indicating that copies received from an outside institution were unaltered as received
- Documents that exceed one page may be verified in a package as a single certified copy if the package will remain intact when filed. To certify this package, individuals must add a signed and dated statement on the first page that indicates the package consisting of X (specify) number of pages is an exact copy of the original information. All subsequent pages must be initialed and dated to verify that each is part of the package.

#### Common Deficiencies

- Incomplete/illegible certified copies, where the data cannot be 100% verified (e.g., an illegible EKG tracing)
- Missing pages from a package

#### **FLOW SHEETS/WORKSHEETS/TEMPLATES**

Staff at CRSs, DAIDS, DAIDS Clinical Trials Networks, or the protocol team may develop flow sheets/worksheets/templates (pre-printed documents) that become part of the research record when used to help organize study documentation and collect clinical trial data.

These documents help ensure CRS staff perform and document all protocol-required assessments. They may serve as the original participant data record and are used in conjunction with hospital records and/or clinic charts to capture participant visits unrelated to research. They are commonly used to record concomitant medication use, AEs, vital signs, inclusion/exclusion criteria/eligibility assessments, and other participant data.

These types of documents must be developed in a way that facilitates detailed source data documentation (i.e., a robust document that consists of more than checkboxes). As examples:

- Inclusion/exclusion checklists should contain fill-in-the-blank fields to add diagnostic test results and clinical values required for eligibility.
- Physical examination checklists should include all body systems and leave extra fields for other non-protocol specific examination requirements.
- Physician assessment worksheets should prompt physicians to assess all required components using protocol-required scales/terminology.

It is important to develop these documents with space for further medical notes and data from routine practice outside of study-specific data/requirements.

CRS staff should establish written procedures that describe CRS processes to create worksheets/templates/flow sheets and outline best practices for their use. Most commonly, these procedures are included in the CRS's source documentation SOP.

#### Common Deficiencies

- Leaving checkboxes unchecked on the document
- Missing signature/initials and dates
- Missing participant identifiers and dates
- Inadequately identifying the individual responsible for each entry on a document that includes entries by multiple CRS staff
- Developing a document that only allows individuals to document study-specific requirements, resulting in participant records that omit standard of care elements

#### **MEDICAL RECORDS**

Medical records are any records that contain any kind of patient medical information (e.g., physical examinations, concomitant medications, signs and symptoms/AEs, diagnoses, laboratory results, diagnostic reports, etc.).

When study visits are conducted in a combined (research/clinical practice) setting, participant research records and practice/clinic/hospital records should always be maintained in one location to ensure that anyone accessing participant records is aware of the combined visits. If this is not possible, it is highly recommended that the participant's practice/hospital/clinic chart indicate they are participating in a study and list the study's point of contact in case questions arise.

CRS staff review participant medical records to ensure they obtain all data that may be relevant to the protocol. CRS staff must have certified copies of medical records from outside institutions and primary care providers if those records support a participant's eligibility, endpoints, or expedited AEs (EAE)/serious AEs (SAEs), or if a DAIDS medical officer requests them while investigating AEs.

Sometimes it is not possible to obtain copies of medical records while a participant is on study. For example, this may occur when a research participant is seen in an out-of-town clinic or hospital and CRS staff cannot access copies of pertinent treatment records despite a signed release of information by the study participant.

In this case, CRS staff would document in the research record that certain medical records are missing and describe the CRS's efforts to obtain the missing records.

#### Common Deficiencies

- Medical records are inaccessible or unavailable (e.g., medical record in use at a different department, without a documented reason) to a monitor, auditor, or other authorized individuals, such as representatives from regulatory authorities.
- A CRS's certified copies from other institution's records are inadequate (e.g., missing pages, unidentified records, etc.).

#### RESEARCH RECORDS

Research records constitute all documents that substantiate data collected and/or are relevant to a participant's in a clinical trial. These may include:

- Informed consent signed by the participant
- Worksheets
- Study product records
- Study-specific questionnaires
- Imaging and laboratory reports
- CRFs, when used as source documents

#### Common Deficiencies

- Data are recorded without being signed/initialed and/or dated.
- Entries for the same data are inconsistent throughout the research record, (e.g., discrepant vital signs recorded in the worksheet and clinical notes on the same date/visit).
- Certified copies from other institution's records are inadequate (e.g., missing pages, unidentified records, etc.)

#### REQUIREMENTS AND BEST PRACTICES FOR DOCUMENTING CLINICAL TRIAL DATA

The requirements and best practices in this section should be used by CRSs when collecting source document data to support and ensure data integrity and participant safety. These practices also confirm compliance with all protocol requirements, applicable regulations, and ICH E6 guidelines.

#### ADDENDA (ADDENDUM/LATE ENTRY)

When source documents are found to be incorrect, incomplete, or otherwise deficient, they need to be corrected and/or completed. Deficient records may be identified by CRS staff during quality management activities or by a monitor during a site visit. CRS staff can correct these documents by recording an additional entry or addendum to the source document.

All additional entries or addenda must be signed and dated in real time by the individual making the entry. Addenda that are not appropriately signed and dated are prohibited because such entries are not verifiable.

When including an addendum to a source document, CRS staff should document the deficiency and the circumstances surrounding the situation (if known) and make sure their signature and the date are as close as possible to the entry.

If research records are missing data and those data are obtained at a later date, CRSs must incorporate the missing data into the research record with supporting notes, signature/initial, and dates.

**CRS staff must NEVER modify previously dated source documents in research records if attempting to resolve deficiencies.** Altering, substituting, or discarding previously dated records is potentially fraudulent.

## ASSENT

CRS staff must record participant assent (paper or electronic) using a written assent form, document the process in the research record, and maintain all original signed and dated assent forms on site. Signatures and dates on the assent form may include those from the participant/LAR, individual who conducted the process, a witness to the assent process, translator, or others according to the requirements of the local Institutional Review Board (IRB)/Ethics Committee (EC).

Documentation (consenter notes) of the assent should:

- Accurately reflect the process.
- Include that assent occurred before any study procedures were conducted.
- Include who participated in the process.
- Clarify that all participant questions were adequately addressed, and that the participant was able to comprehend (limited to their capacity) what it means to participate in the study.
- Include the version of the assent that was used and the time of the assent (if required by the protocol).
- Include if a signed copy of the assent was provided to the participant/LAR, and whether the provided copy was accepted or rejected.

At times, assent cannot be administered due to a participant's circumstances. If a participant is unaware of their diagnosis (e.g., participant is human immunodeficiency virus [HIV] positive) and/or has a developmental delay or intellectual disability, the consenter and the parent/legally authorized representative (LAR) may decide not to obtain assent. In such situations, and others that may depart from norms, CRSs must include detailed records in the source document to ensure that anyone reviewing the documentation clearly understands the decision to deviate from the normal assent process.

Refer to the [Informed Consent of Participants](#) section of the SCORE Manual for additional information.

## CONCOMITANT MEDICATION: NON-STUDY

CRS staff must document participant-or LAR-reported use of concomitant medications, non-study products, and prohibited medications according to protocol requirements and standard of practice. Concomitant medications include but are not limited to, prescription medications, non-prescription or over-the-counter medications (e.g., Tylenol®/acetaminophen, Benadryl®/diphenhydramine), recreational drugs (e.g., cocaine, heroin), as well as vitamins and dietary supplements.

CRS staff are reminded to always include all available information, such as product name, indication, dose, frequency, and start/stop date when documenting concomitant medication use.

## CONFIDENTIALITY

CRS staff must fully inform all participants of the extent that their institution/all parties involved in conducting the clinical trial will keep all participant records confidential. CRS staff must carefully de-identify all participant data if sharing such data outside their site.

This de-identification process must include identifying participants with a code (e.g., patient identification number [PID/PTiD]) and removing all personally identifiable information (PII) such as name (i.e., first name or surname), signature, home address, telephone number, email address, health insurance number, and government-issued identification numbers (e.g., Social Security number, National Health Service number).

Identifiers on original records must never be redacted, even if a new identifier is added to the document (e.g., placing a PID label over a participant's name or vice versa).

If CRS staff must share a record with PII with DAIDS (e.g., death report attached to an SAE submission), a redacted copy of the original report must be submitted.

Non-CRS staff usually do not require information that would connect participants to their research records. For this reason, CRS staff should not routinely use study identification numbers, such as PID/PtID, in hospital charts or medical records used by non-research personnel and/or off-site charts/records.

## CONTRACEPTION: PROTOCOL-REQUIRED

CRS staff should verify current standard of practice and protocol's inclusion criteria for contraception and ensure adequate documentation before randomizing/enrolling participants.

CRS staff must be adequately qualified, trained, and delegated the responsibility to document their counseling participants on the importance of using contraception and available methods, when applicable. Regardless of participants' sexual orientation (i.e., heterosexual, lesbian, gay, or bisexual) or sexual activity (i.e., sexually active or abstinent), it is important for CRS staff performing documentation to consider and/or communicate the following:

- Clinical trials include contraception requirements to reduce/eliminate risk to a fetus
- Avoiding assumptions about participants' sexual activities or interest in parenting a child
- Age does not prevent biologically male participants from fathering children or biologically female participants from becoming pregnant.

If the protocol specifies that participants must agree to practice one or more forms of contraception, staff must document one of the following:

- Methods the participant reported they will use.
- Participant was counseled on the number of necessary contraception methods, provided a list of acceptable forms of contraception, and agreed to use contraception when necessary.
- Participant's lack of reproductive potential due to menopause, sterilization (hysterectomy, oophorectomy, tubal ligation, or vasectomy), or age. (Note: always consult the protocol to determine if self-reporting reproductive potential is acceptable or if documentation is required.)

## DEATH

Preferably, CRS staff should include official documentation (i.e., obituary, death certificate, and/or autopsy report) when reporting a participant's death and include a copy of that documentation in the participant's file to verify the date and cause of death.

If CRS staff is verbally notified of a participant's death, they must record the following in the source document:

- Name of individual reporting the death and their relationship to participant (healthcare provider, family member, partner, friend, etc.)
- Date death was reported to the CRS
- Date of death
- Reported cause of death
- Dates and methods used by the CRS in attempting to obtain official documentation to verify the reported date and cause of death

CRS staff must also review and comply with the DAIDS requirements for EAE/SAE reporting of deaths.

## PROTOCOL DEPARTURES/DEVIATIONS

CRS staff must record all protocol departures/deviations (e.g., enrolling ineligible participants, incomplete laboratory evaluations, incomplete physical assessments, missed visits, etc.) in the participant's research record. If pertinent, CRSs should also document reasons for the departures and attempts to correct and/or prevent the departures from reoccurring. Example scenarios of departures and how to document them appropriately include:

- Missed participant visit: CRS needs to document the visit was missed, the reason for it (if available), and the attempts to locate the participant to request a make-up visit. CRS must also include the means by which they obtained this information (e.g., telephone contact, conversation with relative, other medical records, etc.).
- Clinical trial procedure or medication changes due to clinical judgment (e.g., CRSs must decrease blood volume collected for storage due to participant's anemia): CRS needs to document the reason for the change, actions taken due to the change, communication with the protocol team and IRB/EC (as

necessary), and resolution.

## ENDPOINTS

For study-defined clinical or laboratory-based endpoints, the CRS staff must document the specifics of an event or test result(s) in a participant's research record as required by the protocol. To substantiate a diagnosis, CRSs must include results of all diagnostic evaluations in the participant's research records. They must also include any communications received (i.e., email and/or laboratory/protocol team member notification) when a participant reaches a study-defined, clinical or laboratory-based endpoint.

## ENTRY CRITERIA (INCLUSION/EXCLUSION CRITERIA)

The Principal Investigator (PI)/Investigator of Record (IoR) or appropriately delegated staff must assess and document the protocol's inclusion/exclusion criteria before enrolling/randomizing clinical trial participants. Appropriate forms of documentation include:

- Chart notes that demonstrate that appropriate staff assessed each criterion
- Internal eligibility checklists that:
  - Include inclusion/exclusion criteria that corresponds with the current, approved protocol version.
  - Provide space to address each criterion with supporting documentation.

(Please refer to this section's "Flow Sheet/Worksheets/Templates" entry for information on creating adequate internal documents like checklists).

- Original documents or certified copies of protocol-required diagnostic results and/or medical history (e.g., laboratory result, radiology report, medication history, etc.).

**Note:** Blanket statements on whether a participant meets or does not meet inclusion/exclusion criteria (e.g., "The participant does/does not meet the inclusion or exclusion criteria outlined in the protocol.") are NOT adequate source documentation.

## IDENTIFIERS

CRSs must consistently label all source documents with at least one unique identifier so anyone can verify that documents correspond to a particular participant. Unique identifiers include a participant's:

- Full name (if there are no other participants with the same name at the CRS)
- Hospital identification number
- Medical record number Social Security number
- National Identity number
- PID/SID/PtID
- Two non-unique identifiers in combination

Avoid using identifiers that are NOT unique, such as date of birth, participant initials, and full name (if other participants at the CRS have the same name).

NEVER obliterate identifiers on original documents, even if a new identifier is added to the document (e.g., placing a PID label over a participant's name). If records are being shared with non-authorized staff, CRSs may de-identify copies of records by redacting PII and replacing them with PID/SID/PtID numbers.

## INFORMED CONSENT

Consenters - CRS staff who conduct the informed consent process - must document informed consent in participant research records using a signed and dated written informed consent form (ICF) and a written description of the informed consent process. CRSs must maintain all original signed and dated documents on site. Signatures and dates on the consent form may include the participant/LAR, the consentor, a witness to the consent process, a translator, or others according to local IRB/EC requirements. Check applicable IRB/EC or other local requirements to determine whether ICFs require participants/LARs and consenters to initial all ICF pages.

For informed consent process documentation (consenter notes), consenters should clearly describe the process, and include:

- If the consent occurred before conducting any study procedures
- Who participated in the process (i.e., consentor, participant, translator, etc.)
- If all participant questions were adequately addressed, and that the participant comprehended (limited to their capacity) what clinical study participation entails
- The ICF version used and time of consent (if required by the protocol)
- If a signed copy of the consent was provided to the participant/LAR, and whether the participant/LAR accepted or rejected the copy

In addition, consenters must assess whether participants/their LARs understand the information presented in the ICF and document their assessment in the source documents. Consenters and/or other appropriate CRS staff must clarify any participants' misunderstanding before signing the ICF.

The informed consent process must also include documentation of participants who are unable to consent for themselves and the reason why.

Refer to the "Informed Consent of Participants" section of the SCORE Manual for additional information.

## KARNOFSKY SCORE

CRS staff must review and record the score assigned to a participant at a given point in time in the research record according to protocol requirements. The participant's medical record usually includes data to support the assigned score; if not, note the rationale for the score.

## LABORATORY TESTS: SPECIMEN COLLECTION (RESEARCH AND ROUTINE)

CRS staff must document when any specimens are obtained from participants and include all protocol-required details.

- If the protocol requires the specimen collection time (e.g., for pharmacokinetics), CRS staff must document the time in participant research records.
- If the protocol requires fasting, CRS staff should add the following to the participant's research record:
  - Participant's confirmation that they fasted for more than eight hours, or as specified by the protocol.
  - Specific date and time of the last food and/or fluid intake.

#### LABORATORY TESTS: RESULTS (RESEARCH AND ROUTINE)

All reports must have appropriate participant identifiers and specimen collection dates. Reports must also meet all Good Clinical Laboratory Practice requirements, such as where (i.e., location of laboratory) the test was performed. Refer to the *DAIDS Good Clinical Laboratory Practice Guideline* for details.

CRSs must keep participant laboratory reports with participant records. As with other source documentation, staff must never redact participant identifiers or de-identify an original report.

The Principal Investigator/Investigator of Record (PI/IoR) or other appropriately delegated CRS staff in the delegation of duties (DoD) log, must document their review of laboratory reports. Review documentation must include the significance of results (clinical versus nonclinical), note identified toxicities, and be available in the research chart. Refer to the "Toxicities: Grading (Adverse Events, Signs and Symptoms, Laboratory results)" section below for details on grading toxicities.

When reporting lymphocyte counts/percentages, CRSs may include the corresponding complete blood count (CBC) with differential to verify total lymphocyte count, depending on the laboratory's reporting format.

For batched and/or blinded research laboratory analyses, CRS staff only have to document results in a participant's research records if the laboratory disclosed unblinded results to manage the participant, terminate a study, or re-randomize/re-allocate step assignment.

#### MEDICAL HISTORY: GENERAL AND HUMAN IMMUNODEFICIENCY VIRUS (HIV) SPECIFIC

As defined by the protocol, written medical history documentation should include, but not be limited to, diagnoses, signs and symptoms, medications, and tests. CRSs are allowed to interview participants and document their verbal history in research records, as long as the documentation includes the source (individual providing the history).

In addition, CRSs should obtain reports of laboratory tests, diagnostic procedures, and examinations as necessary to substantiate the participant's reported medical history. Medical chart notes or letters from a referring healthcare provider are acceptable forms of documentation.

To diagnose HIV, refer to the number and types of tests required or permitted for use by protocol, as entry criteria may have more specific requirements.

#### PRESCRIPTIONS

CRSs may only dispense study product after the pharmacist of record receives a signed prescription from the PI/IoR or a licensed clinician delegated for this activity on the DoD log. Prescribers must be listed on the current

Form FDA 1572 for investigational new drug (IND) studies or on the authorized prescribers list for non-IND studies for a given protocol at the participating CRS. All prescribers must be clinicians authorized to prescribe in the CRS's jurisdiction.

Documentation that a prescription for study product was completed, such as a chart note indicating prescription was written or copies of the prescriptions that were sent to the DAIDS Pharmaceutical Affairs Branch-approved investigational pharmacy, must be available in a participant's research records.

Prescriptions must include the date of issue, participant identifier (e.g., name or PID), network name and protocol number, treatment assignment (e.g., SID, PtID, or kit number), study product name (in a blinded fashion for blinded studies), dose, strength, formulation, administration route, quantity or volume to be dispensed, directions for use, and authorized prescriber's signature and date of signature. Prescriptions may be written with refills, if allowed per local laws and regulations.

Prescriptions must be either handwritten with dark (blue or black) ink, typed, or computer generated. Signatures on the prescriptions should be handwritten or electronically signed (using a 21 CFR Part 11-compliant system). Prescribers may not use signature stamps, sign blank prescription forms, or post-date prescriptions (e.g., it is not acceptable for a prescription written in January to have a February date).

The authorized prescriber must ensure that the prescription is written in accordance with the protocol's essential aspects and requirements and local laws and regulations.

#### Documenting Changes in Study Treatment:

- Must document any study product status change in detail to justify the change as recorded on the CRF
- Must include the reason for the change and the actual dose change in entries regarding dose modifications
- Must include the reason/rationale in notes regarding holding study product or reinstituting study product and dose

#### PROCEDURES: DIAGNOSTIC, THERAPEUTIC, SURGICAL AND OTHERS.

If CRS staff request any procedures be conducted on a participant, it must be accompanied with appropriate documentation that describes the procedure, names the individual who performed the procedure, and why the procedure was requested (i.e., protocol mandated). CRS staff must document all results and interpretations of diagnostic procedures in the source document, whether required by the protocol or not.

#### QUESTIONNAIRES: COMPLETED BY PARTICIPANT/LAR AND/OR STUDY PERSONNEL

Protocols may require CRSs to complete different types of questionnaires (e.g., health status questionnaires, neuropsychology tests, nutrition surveys, quality of life questionnaires, participant diaries, etc.) during study conduct.

CRSs must provide documentation when a protocol-mandated questionnaire is provided or administered to a participant/LAR according to protocol requirements.

If the participant/LAR completes the questionnaire, note the date it was provided to the participant/LAR to complete and the date it was completed in the participant's research record. Note: if a protocol requires CRS staff to remain blinded to information on completed questionnaires the document must be returned to the unblinded study staff to be stored securely.

If someone other than the participant/LAR completes a questionnaire, always document who completed it and the reason it was incomplete.

If delegated CRS staff complete a questionnaire, they must sign/initial and date all questions and/or sections that they completed and indicate the method used to complete the questionnaire (i.e., participant interview by staff).

Completed questionnaires are considered source documents and must always be retained as part of participant charts/research records.

## SCREENING

Screening is defined as any procedure done to determine a potential study participant's eligibility before enrolling them in a clinical trial. Protocols outline more specific screening procedures, but all studies require CRSs to obtain proper informed consent from participants before screening them for study participation. CRSs must document screening procedures in participant research records.

The PI/IoR or designee must maintain a screening log that lists all potential participants screened for a protocol. The CRS is not required to keep names from broad medical records/database reviews on the screening log; however, it is good practice to include them to verify that potential participant selection was unbiased for a study.

## STUDY PRODUCT MANAGEMENT

Correct and accurate study product management, as specified by the protocol, is to be documented. Documentation of this data can be recorded in the participant's research record and/or pharmacy records, such as study product preparation records, dispensing, and accountability records.

CRS staff must document participant receipt and adherence of oral study product and/or administration of parenteral (e.g., intravenous, intramuscular) study products in the source documentation (e.g., dispensing/administrative worksheets, pharmacy records).

It is important to remember that documentation includes quantitative and qualitative data as follows:

- Quantitative data support the quantity of an item, such as amount of study product dispensed and/or returned (if any), the amount administered to the participant (regardless of formulation), and/or the number of missed/non-administered doses.
- Qualitative data are descriptive and are considered to be:
  - Instructions for taking or administering study product provided to and reviewed with the participant.
  - Details regarding how a parenteral study product would be administered (e.g., length of

time, route of administration).

The pharmacist of record must have an established method to account for all study products. At a minimum, accountability records must be protocol- and study product lot-specific, and these records must be used to document the receipt, management, and final disposition of all study products received. The requirements and additional information regarding study product management are outlined in the Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks.

#### TOXICITIES: GRADING (AES, SIGNS AND SYMPTOMS, LABORATORY RESULTS)

All toxicities and/or signs and symptoms, whether assessed by a clinician or reported by the participant, must be documented in the participant research record along with an assessment of the grading and clinical significance. This documentation must include:

- Signature/date of the individual completing the grading and clinical significance assessment
- A numerical grade that corresponds to the DAIDS AE Grading Table; or
- A written description for those toxicities and/or signs and symptoms that do not appear in the table, which corresponds to the DAIDS AE Grading Table's definitions

CRS staff are not required to record grades in participant research records for non-reportable AEs that are not clinically significant (NCS); however, staff need to document they assessed the event and determined it was NCS.

If non-study staff document toxicities and/or signs and symptoms, delegated CRS staff must record:

- Event assessment, including grade and/or written description
- The event's relationship to a study product if the event is reportable as an EAE or SAE. (e.g., if a participant is evaluated for a stroke, the research clinician must document the grade in the research record and, since the event is an EAE or reportable SAE, the relationship of the event to the study product).
- Documentation that supports the determination of the relationship of any EAE or SAE to the study product

The protocol will specify whether EAE or SAE reporting is required, including the intensity or level of AE reporting.

#### TRANSFERRING PARTICIPANTS

CRSs should have an established process (e.g., SOP) regarding the requirements for transferring participants to other CRSs. CRS staff should refer to the specific DAIDS Clinical Trials Network's procedure, such as an SOP, Study-Specific Procedure (SSP), and/or Manual of Operations/Procedures (MOP), before transferring a participant and document the entire process.

The receiving CRS must obtain IRB/EC approval if applicable, and ensure the participant is re-consented before performing any study procedure.

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|----------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|-------------------------------|
|  National Institute of<br>Allergy and<br>Infectious Diseases | Document Number:<br><b>DAIDS-OCS-A28-MAN-00014</b> | Revision Number:<br><b>01</b> |
| Division of AIDS                                                                                                                             | Effective Date:<br><b>16 Aug 2025</b>              | Page:<br><b>18 of 19</b>      |
| Document Title: <b>SCORE Manual: Appendix Source Documents Requirements</b>                                                                  |                                                    |                               |

Original participant research records must be kept with the transferring CRS, and the transferring CRS must provide certified copies to the receiving CRS according to any applicable requirements (IRB/EC or local laws and regulations).

#### VITAL SIGNS AND OTHER ASSESSMENTS

The protocol must specify the vital signs (e.g., temperature, pulse, respirations, etc.) and other assessments (e.g., physical examination, height, weight, body surface area, head circumference, etc.) that CRSs must collect/perform during the study and at each study visit(s). Appropriate documentation of these assessments includes recording the actual result of the assessment (including the appropriate unit [e.g., Fahrenheit, Centigrade, beats per minute]) and any other protocol-required specifics (e.g., oral/axillary temperature monitoring).

All abnormal results must be assessed in a timely manner per the site's internal SOP and/or as described in the protocol, and properly documented by a delegated clinician.

## REVISION SUMMARY

| Version/<br>Revision | Summary of Changes                                                                                                                                                                                                                                                                                                                                           |
|----------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1.0                  | Original Version and became effective on 1/19/2021.                                                                                                                                                                                                                                                                                                          |
| 2.0                  | <p>Pg 3 – Removed duplicate paragraph of text from Case Report Forms Used as Source documents section.<br/>Version became effective on 5/4/2022.</p> <p>Pg 6 – Certified copied language updated to provide details on how a site may verify a document package (several pages) as a single certified copy if the package will remain intact when filed.</p> |
| 3.0                  | <p>Pg. 3,4 – Clarified requirements for all handwritten and electronic source documentation as well as requirements for using CRFs as source documentation.<br/>Version became effective on 10/2/2023.</p>                                                                                                                                                   |
| 4.0                  | <p>Pg 20 – Clarified requirements for documenting grading of severity and clinical significance of AEs for reported/observed toxicities and signs/symptoms.</p> <p>Clarified requirements for documenting clinical significance of laboratory results.<br/>Version became effective on 6/10/2024.</p>                                                        |
| 01                   | DAIDS-OCS-A28-MAN-00014 rev 01 is the first revision of this manual in MasterControl. The document numbering and document format have been updated to reflect current requirements. Removed language to align language as required by current Executive Orders.                                                                                              |