
Division of AIDS (DAIDS) Site Clinical Operations and Research Essentials (SCORE) Manual: Source Documentation

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Source Documents

The International Council for Harmonisation (ICH) Good Clinical Practice (GCP) requirements (“ICH E6”) guidelines define source data and source documents as:

- **Source Data (1.51):** “All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies).”
- **Source Document (1.52):** “Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial). Original Medical Records (1.43) can also be used to refer to Source Document.”

Source documents serve to:

- Substantiate clinical trial data integrity and confirm recorded observations.
- Confirm compliance with all protocol requirements, including safety parameters, all applicable regulations, and ICH E6 guidelines.
- Act as an audit trail that allows inspectors to recreate a clinical trial’s progress.

Requirements for Source Documents and Good Documentation Practices

The Principal Investigator (PI)/Investigator of Record (IoR) must ensure that any Clinical Research Site (CRS) staff with delegated responsibilities for generating, recording, reviewing, and maintaining DAIDS clinical trial data or records comply with this section’s requirements, any applicable DAIDS requirements, local laws, applicable regulations, Institutional Review Board (IRB)/Ethics Committee (EC) as well as institutional requirements, policies and procedures. CRSs must always follow the most stringent requirements. For the purposes of this document, the terms “data” and “records” encompass paper and/or electronic versions.

Source documents include a range of documents from various sources, including paper (hard copies), electronic, magnetic media, optical records, scans, x-rays, and electrocardiograms (EKGs). Multiple CRS staff often generate and review these documents over a long period of time, which may create challenges for adhering to Good

Documentation Practice (GDP) and potentially impact data quality and integrity, which are essential to regulatory authority decision-making around clinical trial conduct. The quote, **“If it is not documented, it did not happen.”** is internationally recognized in clinical trials and indicates the importance of documenting data generated during a clinical trial.

According to ICH E6 (4.9), “the investigator/institution should maintain adequate and accurate source documents and trial records that include all pertinent observations on each of the site’s trial participants. Source data must be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (e.g., via an audit trail).” All CRS staff must protect confidentiality of records that could identify participants in accordance with all applicable regulatory requirements.

Attributable, Legible, Contemporaneous, Original, Accurate, and Complete (ALCOA-C) Principles

The term ALCOA-C is a well-known methodology designed to help individuals working in clinical trials achieve and maintain data quality and integrity. The ALCOA-C methodology is defined as:

Attributable: Individuals who generate, capture or correct data must record, initial/sign, and date their entries to clearly identify who was responsible for documenting the data and when. The PI/IoR must also maintain a delegation of duties (DoD) log where duties are delegated and each delegated staff provides their initials and signatures. This helps identify/link the signature/initials next to the entries to the individual who made the entry. Refer to the SCORE manual’s [Clinical Research Site Personnel Qualifications, Training and Responsibilities](#) section for additional DoD information.

All individuals who generate/capture electronic clinical trial data (including data, findings, observations, and related documents) must have a unique log-in identification (ID) and password to ensure the system audit trail records their actions. Data must also be marked with appropriate identifiers (e.g., participant number, protocol number, sample identification). Requirements related to generating data and records in electronic systems are detailed in the 21 Code of Federal Regulations (CFR) Part 11 and applicable in-country regulations. Refer to the SCORE manual’s [Electronic Systems](#) section for additional information.

Because more than one individual may participate in data generation/collection, records must identify all parties who participated in the process. For example, when a nurse and physician are involved in a participant’s consent process, both user IDs should be recorded.

CRS staff should ask the following questions to verify attributability of the data:

1. Is it clear who documented the data?
2. Is/are the signature/initials unique to the individual responsible for the documentation, and are they used consistently across documents?
3. Is it possible to identify who wrote/recorded the data by comparing the signature/initials to those on the DoD log when the signature/initials is/are not legible?
4. Are pertinent identifiers (e.g., participant, protocol, sample identification) present in the record?

Legible: All data must be recorded legibly and permanently in a durable medium to ensure data quality, integrity, and longevity. Handwritten and printed documents must be easy to read by the author and other parties (e.g., monitors, auditors, inspectors). CRSs should consider the type of paper on which clinical trial data are being generated/printed, to prevent data from fading over time (e.g., do not use thermal paper). CRSs must not use pencil and/or ink that can be easily erased without tracking the change.

CRS staff should ask the following questions to verify data are legible:

1. Can an individual read the handwritten or typed data?
2. Was paper and/or ink used that is permanent and appropriate for long-term storage, or is it prone to fading (thermal paper) over time?
3. Will the system used to store data be accessible during the course of the clinical trial and afterward (i.e., format readable for years to come)?

Contemporaneous: All data must be recorded when it is generated and must always include a signature/initials and date/time stamp that proves the documentation was performed in real time. Records must have a clear narrative and can be placed in the correct timeframe among the flow of events to avoid misinterpretation and ensure data credibility. Source documents must not be pre-filled/completed with expected results prior to execution and must never be backdated. CRSs should record any missing/omitted data as an addendum/late entry and clearly indicate the entry date and data source.

CRS staff should ask the following questions to verify the data are contemporaneous:

1. Does it clearly identify the date/time the data were generated?
2. Is the data recorded in the correct timeframe?
3. Is it a late entry? Is it clearly identified as such with appropriate dating?

Original: The original document is the **first** recording of the data (source or raw data) and is therefore the most accurate and reliable. Any paper or electronic system used to generate clinical trial data (recorded for the first time) is considered the source or raw

data. Original source documents may be medical/staff notes, participant diaries, notebooks, laboratory reports, and email messages. While even sticky notes or a scrap of paper (if it is the original form on which relevant study data are recorded) may be source documents, DAIDS strongly advises against using these mediums to ensure clear, structured records that may not include critical identifiers such as a participant's identification number (PID/PtID), signatures (attributable), and dates (contemporaneous) and can be easily lost/unintentionally discarded. Transcriptions from other sources to participant records are not considered source documents since this is not the first place data was recorded.

CRS staff should ask the following questions to verify whether data are original:

1. Is this document the first place where the data was recorded?
2. Was the data transcribed from another source?
3. Is the document a copy?
4. Has the document been altered?

Accurate: To ensure integrity, all data must be consistent, factual, and error-free throughout the document. All parties must follow GDP if data edits are required.

CRS staff should ask the following questions to verify if the data are Accurate:

1. Is conflicting data recorded elsewhere?
2. Are corrections adequately identified and supported?

Complete: Data should be final, with no missing information or pages. The document must be complete until that point in time.

CRS staff should ask the following questions to verify if the data are Complete:

1. Are data complete (per protocol requirements)?
2. Are there any missing pages or elements?

Types of Source Documents

As discussed, a source document is any record in which data are recorded for the first time. All CRSs conducting DAIDS clinical trials must have an established standard operating procedure (SOP) for source documentation (CRS-specific and/or study-specific), determining in advance whether they plan to rely on the electronic or paper record to perform regulated activities.

Case report forms (CRFs) may be used as source documents, but in this instance, the protocol should prospectively define which data may be treated in this way. As per ICH E6 (6.4.9; Clinical Trial Protocol), “a description of the trial design should include the

identification of any data to be recorded directly on the CRFs (i.e., no prior written or electronic record of data), and to be considered to be source data.” As in their source documentation SOP, the CRS must document whether CRFs will be used or not as source documentation.

There are many types of source documents, and a few are defined here.

Paper-based Records: Hospital records, clinical charts, research charts, and laboratory/image reports are some records that CRSs may use as source documentation. These types of records can include progress, nursing, or clinic notes that contain participant medical information and may or may not be related to the clinical trial. Paper-based records must be maintained in forward or reverse chronological order.

Certified Copy: As per ICH E6 (1.63): “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.”

There may be occasions where the original document that supports the study data are unavailable due to being maintained elsewhere (e.g., at another institution). In this instance, a certified copy of the source document would be acceptable. A certified copy must be signed or initialed and dated by the individual making the copy and contain a statement verifying that the copy is an exact replica of the original document. It is recommended for the CRSs to have a documented certified copy process or procedure in place.

The following are examples of when a certified copy may be required:

- A copy taken from an EKG tracing printed on thermal paper that will fade over time. The certified copy will make the data available for a longer period, as required.
- Copies of a participant medical chart from an external institution to support participant eligibility and/or an adverse event. The certified copy would be the source document at the CRS, as the external institution’s medical chart cannot be retained at the CRS.

Electronic Records: When users enter data directly into a computerized/electronic system (e.g., computer, smartphone, electronic patient-reported outcome or diary), the electronic record (and any associated signature) in that system is the original source document. The system must comply with 21 CFR Part 11 and any other regulatory requirements. Please refer to the DAIDS policy, [Electronic Information Systems](#), for additional information and requirements on the use of electronic records.

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

Certified hard copies of EMRs are not required if the original electronic record (and any associated signature) is maintained and complies with procedures and controls designed to ensure the authenticity, integrity, and the confidentiality of the electronic records and signatures (as appropriate).

A paper record (printout/hard copy/"print screen") of the original electronic record is considered to be a copy. However, some CRS staff may use systems/computer programs, such as MS Word/Excel, which cannot keep reliable data with user access control, maintain an adequate audit trail to provide evidence of any changes made to the data, or be backed up regularly. In these instances, the data must be printed, signed, and dated by the individual who electronically generated it. In this case, the paper is considered the source document and must not be discarded/replaced by a new printed, signed, and dated document. Any required updates to previously recorded data must be documented as a late entry.

While the U.S. Food and Drug Administration (FDA) does not intend to assess full compliance of EHRs with 21 CFR Part 11, it may assess components for certain elements of 21 CFR Part 11. For more information on best practices for using data from EHRs in FDA-regulated clinical investigations, refer to the FDA's industry guidance: *Use of Electronic Health Records Data in Clinical Investigations* and the DAIDS policy, *Electronic Information Systems*.

Electronic Signatures: Electronic and paper records may use electronic signatures if the proper computerized systems and certifications/agreements are in place. To comply with 21 CFR Part 11, the CRS must inform the FDA that they intend to use electronic signatures and that they certify them to be the legally binding equivalent of the individual's handwritten signature. Per 21 CFR Part 11, signed electronic records must contain information associated with the signing that clearly indicates all of the following: (1) the printed name of the signatory; (2) the date and time when the signature was executed; and (3) the meaning (e.g., review, approval, responsibility, or authorship) associated with the signature.

The appendix [Source Documentation Requirements](#) provides additional information about types of source documents and requirements for generating data.

The requirements for documentation, record-keeping, and record retention apply to all records. The SCORE manual's [Essential Documents](#) section provides source document storage and retention requirements.

Error Correction

When generating data, errors to the original entry may occur and must be corrected as soon as they are identified. When possible, corrections must be performed in real time to avoid additional errors or data discrepancies within the same record or across multiple records. Error correction must be performed by the individual who created the original entry or by an authorized individual without obscuring the original entry. The use of Wite-Out® or Tipp-Ex® is not an acceptable practice.

Error corrections must be performed as follows:

- Draw a single line through the incorrect information.
- Insert the correct information.
- Initial, date, and document the reason for change (if not evident).

Late-entry/Addendum

Sometimes, new data must be added after the original record was generated. Addenda or changes must be dated and initialed using the date the new data were added. When creating addenda to source documents, document the deficiency and the circumstances surrounding the situation (if known). **In an attempt to resolve deficiencies, CRS staff must NOT modify previously dated source data in research records.** Altering, substituting, or discarding previously signed and dated records is potentially fraudulent.

Clinical research site staff must never destroy original documents (source), including certified copies, even if they are updated through a late entry.

Access to Source Documents and Participant Confidentiality

Upon request of the monitor, auditor, IRB/EC, or regulatory authority, the investigator or institution must make all requested clinical trial-related records available for direct access, including hospital records and past medical histories. As per ICH E6 (1.21), direct access is the “permission to examine, analyze, verify, and reproduce any records and reports that are important to the evaluation of a clinical trial. Any party (e.g., domestic and foreign regulatory authorities, sponsor’s monitors and auditors) with direct access should take all reasonable precautions within the constraints of the applicable regulatory requirement(s) to maintain the confidentiality of subjects’ identities and sponsor’s proprietary information”. CRS staff must ensure participants are adequately informed of the extent to which confidentiality of records identifying them will be maintained, and that participants must

consent in writing by signing the study informed consent form to grant direct access for review of their medical records to inspectors and DAIDS staff and their representatives. Any data shared outside of the CRS must be identified by a code (e.g., PID/PtID). In addition, any personal identifiers such as name (in full or part; i.e., first name or surname), signature, home address, telephone number, email address, health insurance number, or government issued identification number (e.g., Social Security number, national health service number) must be redacted.

Never redact identifiers on original records, 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 a record with a PII must be shared with DAIDS (e.g., death report to be submitted attached to the serious adverse event submission), submit a redacted copy.

Additional Good Documentation Practices

This section provides additional GDPs that help CRS staff prevent errors and/or avoid generating inaccurate data.

Use a consistent date and time format throughout documents. The handwritten or typed date format (that is not programmed and generated from an electronic system) is any combination of the use of two digits for day, three letters for month (or the full month spelled out), and four digits for year with or without hyphens/spaces, as long as the reader can identify the day, month, and year. Use the 24-hour clock format 00:00 to 23:59 (e.g., 1:00 PM recorded as 13:00) to format the recorded time, whether handwritten or typed (e.g., pharmacokinetic sample collection, dosing time). However, if a 12-hour clock format is used, time must be clearly designated as either AM (am) or PM (pm), capitalized or lowercase.

Every required document field should have an entry. Otherwise, alert the reader that there is no entry for that field. For example, if no data or text can be entered, consider using the following annotations (abbreviated or spelled out):

- “N/A” or “NA” if the information is not applicable.
- “UNK” if the information is unknown.
- “NAV” if the information is not available.

Blank pages or spaces must be marked as such (e.g., “This page is intentionally blank”) or otherwise noted (e.g., strike-through) to clarify that a page is intentionally blank.

Acronyms and abbreviations, if used, must adhere to established standards and/or project specifications (e.g., published standard medical practice abbreviations).

Clinical Research Site Data Management Requirements

After generating and recording data, the PI/IoR must ensure data are transcribed/reported in the paper, optical, or electronic CRF (eCRF). The CRF design includes fields to record all protocol-required information that must be reported to DAIDS for each clinical trial.

It is important for DAIDS clinical trials to be of the highest quality by collecting complete and accurate clinical trial data and ensuring participant safety. The DAIDS policy, *Electronic Information Systems* provides the requirements for data management operations and overall data management systems that all CRSs conducting DAIDS clinical trials must follow.

When cases of incorrect or inconsistent data in a CRF occur, the data management center, contract monitors, CRS quality management, or others will generate queries. Any data reported in the CRF must meet ALCOA-C principles and be supported by a source document. As required for source documentation, changes or correction must be traceable, not obscure the original entry (i.e., an audit trail should be maintained), be signed/initialed, dated, and include a clear explanation for the change (if not evident).

Each DAIDS Network and/or protocol will provide additional information regarding data collection and reporting in the CRF. The network or protocol will also provide timelines for completing/resolving the CRF and query(ies).

Appendices

1. [Source Documents Requirements](#)

References

1. [U.S. Code of Federal Regulations, Title 21, Parts 11, 50, 54, 56, and 312](#)
2. [U.S. Code of Federal Regulations, Title 45, Part 46 and Subparts](#)
3. [International Council for Harmonisation Good Clinical Practice \(ICH E6\)](#)
4. [DAIDS Electronic Information Systems \(EIS\) POL-A15-OPC-013 policy](#)
5. [FDA Use of Electronic Health Record Data in Clinical Investigations, Guidance for Industry, 2018](#)
6. [FDA Guidance for Industry, Electronic Source Data in Clinical Investigations, 2013](#)
7. [FDA Guidance for Industry, Electronic Records: Electronic Signatures – Scope and Application, 2003](#)
8. [FDA General Principles of Software Validation; Final Guidance for Industry and FDA Staff, 2002](#)
9. [FDA Guidance For Industry - Computerized Systems Used In Clinical Trials, 1999](#)