SCORE Manual Detailed Summary of Changes

Section	Current	New	Rationale
Introduction to DAIDS Systems Revision 02	Pg. 2- **Note:** To access trainings within the DLP, the user account must reference an active DAIDS CRS number. To create a user account, follow these steps: 1. Access the DAIDS Learning Portal and select "Create New Account." 2. Complete the "New Account" form including your DAIDS CRS number. 3. DLP support will provide access to DLP.	**Note:** To access trainings within the DLP, new users will need to have either a Login.Gov account or use a NIH PIV card. To create a user account, follow these steps: 1. Access the DAIDS Learning Portal and select "How to create your Account." 2. Create Login.gov account. 3. Go back to DAIDS Learning Portal and enter Log in credentials. Contact DLP Support in case of questions, support-daidslearningportal@niaid.nih.gov	Align instructions with current process to create a Login.gov account.
	Pg. 5 - CRS staff must electronically upload and track the site's essential regulatory documents and PI/IoR information as described in the Protocol Registration Manual.	CRS staff must electronically upload and track the site's essential regulatory records and PI/IoR information as described in the Protocol Registration Manual.	Updated to align terminology with ICH GCP E6(R3). Corrected placement of hyperlink to RSC site.
	Pg. 9 - No training is required to gain access. 1. DAIDS Learning Portal and select "Create New Account." 2. Complete the "New Account" form including your DAIDS CRS number. 3. DLP support will notify users of access to DLP. 4. Contact DLP Support in case of questions.	No training is required to gain access. • Access the DAIDS Learning Portal and select "How to create your Account." • Create Login.gov account. • Go back to DAIDS Learning Portal and enter Log in credentials • Contact DLP Support in case of questions.	• Updated hyperlink to DAIDS Learning Portal • Align instructions with current process to create a Login.gov account.

Investigator Responsibilities Revision 01	Pg. 5 – Essential documents such as source documents, required communications, and/or IRB/EC and RE/RA approvals… PIs/IORs are responsible for maintaining copies of completed, signed and dated essential documents… Please see the SCORE Manual's Essential Documents and Source Documentation sections for details.	Essential Records such as source records, required communications, and/or IRB/EC and RE/RA approvals… PIs/IORs are responsible for maintaining copies of completed, signed and dated essential records… Please see the SCORE Manual's Essential Records and Source Records and Documentation sections for details.	Updated to align terminology with ICH GCP E6(R3). Updated associated hyperlinks to Essential Records and Source Records and Documentation.
	Pg. 6 - Ensure all essential documents are filed and stored according to the SCORE Manual's "Essential Documents" section, ICH E6 (section 8.0), applicable regulations, and institutional requirements.	Ensure all essential records are filed and stored according to the SCORE Manual's "Essential Records" section, ICH E6 (section 8.0), applicable regulations, and institutional requirements.	
	Pg. 8 - As required by ICH E6 (8.2.6) as part of the essential documents, agreements between parties involved in clinical trial must be in place.	As required by ICH E6 (8.2.6) as part of the essential records, agreements between parties involved in clinical trial must be in place.	
Clinical Research Site (CRS) Personnel Qualifications, Training, and Responsibilities Revision 01	Pg. 5 - that the CRS keeps on file documentation that personnel were trained on all study procedures before being delegated …	the CRS keeps on file documentation that personnel were trained on relevant study procedures before being delegated…	Clarification that protocol training is tailored to the procedures delegated by the IoR.
	Pg. 7 - The PIs/IoRs must record duties/tasks they are delegating to the individuals, under ~~his~~ direct or indirect supervision, only after completion of all protocol-specific training. Each individual must personally sign (i.e., handwritten signature), initial, ~~and date~~ the DoD log in the corresponding columns for the delegated duties/tasks at the time the delegation is made. CRS staff may sign the	The PIs/IoRs must record duties/tasks they are delegating to the individuals, under their direct or indirect supervision, only after completion of all protocol-specific training. Each individual must personally sign (i.e., handwritten signature), initial the DoD log in the corresponding columns for the delegated duties/tasks at the time the delegation is made. If using handwritten signature and initials, individuals must record all variations of both	Provided additional guidance regarding documentation to ensure all variations of signatures are attributable for delegated staff.

Clinical Research Site (CRS) Personnel Qualifications, Training, and Responsibilities Revision 01 (cont'd)	DoD with an electronic signature (eSignature), ~~but to do so,~~ the CRS must have an established procedure in place for using eSignatures…	(ideally on a signature log) they will be using when documenting the data to ensure that all documentation is attributable to respective site staff. If CRS staff sign the DoD with an electronic signature (eSignature), the CRS must have an established procedure in place for using eSignatures…	
	Pg. 8 - Similar to participant research documents and other essential documents…	Similar to participant research records and other essential records…	Aligned terminology with ICH GCP E6(R3)
	Pg. 9 - Change requests are to be sent through the authorized Business Official at the grantee institution ~~by email or formal letter on official letterhead…~~	Change requests are to be sent through the authorized Business Official at the grantee institution via the eRA Commons Prior Approval Module…	Updated process appropriate methods for submission of changes of key personnel for approval (core-funded clinical trial units and associated sites only)
Appendix – Guidance on Completion of DoD Log Revision 02	Pg. 2 - **Name, Signatures, and Initials** The PI/IoR, CRS staff, and other individuals who have been delegated significant study duties/tasks use the same signature and initials, as provided on the DoD Log, when signing and initialing source documentation, case report forms and any study-related records (essential documents). **Signatures** CRS staff and other individuals assigned a duty/task must sign using a full signature, in the column next to their name. This signature will be used to later compare entries made by them in essential documents. Note that some regions require a signature in addition to the English-language signature; in this case, CRSs must capture both signatures on the DoD log. **Initials** Individuals enter their initials as they will appear on any essential documents. Initials must be unique for all CRS staff and other individuals (e.g., if two individuals have the initial "NM", one staff must also use a middle initial).	**Name, Signatures, and Initials** The PI/IoR, CRS staff, and other individuals who have been delegated significant study duties/tasks use the same signature and initials, as provided on the DoD Log, when signing and initialing source documentation, case report forms and any study-related records (i.e., essential records). **Signatures** CRS staff and other individuals assigned a duty/task must sign using a full signature, in the column next to their name. This signature will be used to later compare entries made by them in essential records. Note that some regions require a signature in addition to the English-language signature; in this case, CRSs must capture both signatures on the DoD log. **Initials** Individuals enter their initials as they will appear on any essential records. Initials must be unique for all CRS staff and other individuals (e.g., if two individuals have the initial "NM", one staff must also use a middle initial).	Aligned terminology with ICH GCP E6(R3)

Appendix – Guidance on Completion of DoD Log Revision 02	Pg. 4 – 4. Obtain and document medical history (source documents) 7. Manages regulatory documents/submissions 25. Maintain essential documents 26. ~~Other (specify):~~	4. Obtain and document medical history (source records) 7. Manages regulatory records/submissions 25. Maintain essential records **26.** Translation of Informed Consent Documents (as needed)	Added new responsibility in the event site staff are designated to translate any ICF documents.
	Pg. 6 - **Principal Investigator/Investigator of Record End-of-Study Declaration** At the end of a study, the PI/IoR will sign and date the DoD Log in the designated area after reviewing all entries for accuracy. They must retain the current, completed DoD log and all previous original DoD log versions at the CRS according to the DAIDS requirements described in the SCORE Manual's Essential Documents section. **Version Control** CRSs are required to maintain version control of the DoD log and ensure the version is documented on each page of the record (i.e., footer). In case the document is revised, for example adding a new field, a new version number should be included. The first final version of a document should be Version 1.0 and should include the date when the record becomes final/effective. Subsequent revised documents will have an increase of "1.0" in the version number (2.0, 3.0, etc.).	**Principal Investigator/Investigator of Record End-of-Study Declaration** At the end of a study, the PI/IoR will sign and date the DoD Log in the designated area after reviewing all entries for accuracy. They must retain the current, completed DoD log and all previous original DoD log versions at the CRS according to the DAIDS requirements described in the SCORE Manual's Essential Records section. **Version Control** CRSs are required to maintain version control of the DoD log and ensure the version is documented on each page of the record (i.e., footer). In case the record is revised, for example adding a new field, a new version number should be included. The first final version of a record should be Version 1.0 and should include the date when the record becomes final/effective. Subsequent revised records will have an increase of "1.0" in the version number (2.0, 3.0, etc.).	Aligned terminology with ICH GCP E6(R3)
Appendix – DAIDS Delegation of Duties Log Revision 03	Pg. 3 – **Significant Study-related Duties** 4. Obtain and document medical history (source documents) 6. Manage Regulatory Documents/Submissions 24. Maintain Essential Documents	**Significant Study-related Duties** 4. Obtain and document medical history (source records) 6. Manage Regulatory Records/Submissions 24. Maintain Essential Records	Aligned terminology with ICH GCP E6(R3)

Clinical Research Site Facility Requirements (Clinic, Laboratory and Additional Locations) Revision 01	Pg. 3 - All previous equipment maintenance records must be filed at the CRS and retained for the duration of the study, per the Essential Documents section…	All previous equipment maintenance records must be filed at the CRS and retained for the duration of the study, per the Essential Records section…	Aligned terminology with ICH GCP E6(R3)
	Pg. 6 - Documentation of the lot numbers and expiration dates of the POCT kits in the participant source documents	Documentation of the lot numbers and expiration dates of the POCT kits in the participant source records	
Source Records and Documentation Revision 01	Document Title - Division of AIDS (DAIDS) Site Clinical Operations and Research Essentials (SCORE) Manual: Source Documentation Pg. 2 – Section title: Source Documents ~~**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 medicotechnical departments involved in the clinical trial). Original Medical Records (1.43) can also be used to refer to Source Document."~~ Source documents serve to: …	Division of AIDS (DAIDS) Site Clinical Operations and Research Essentials (SCORE) Manual: Source Records and Documentation Source Records **Source Records (ICH Glossary):** "Original documents or data (which includes relevant metadata) or certified copies of the original documents or data, irrespective of the media used. This may include trial participants' medical/health records/notes/charts; data provided/entered by trial participants (e.g., electronic patient-reported outcomes (ePROs)); healthcare professionals' records from pharmacies, laboratories and other facilities involved in the clinical trial; and data from automated instruments, such as wearables and sensors." **Metadata (ICH Glossary):** The contextual information required to understand a given data element. Metadata is structured information that describes, explains or otherwise makes it easier to retrieve, use or manage data. For the purpose of this guideline, relevant metadata are those needed to allow the appropriate evaluation of the trial conduct. Source records serve to: …	Aligned terminology, guidance, and references with ICH GCP E6(R3)

Source Records and Documentation Revision 01 (cont'd)	**Requirements for Source Documents and Good Documentation Practices** Pg. 3 - Source documents include a range of documents from various sources… According to ICH E6 (~~4.9~~), "the investigator/institution should maintain adequate and accurate source documents and trial records…	**Requirements for Source Records and Good Documentation Practices** Source records include a range of documents from various sources… ICH E6 (C.2.1) requires that essential records, including source records, be identifiable and version controlled (where appropriate), and should include authors, reviewers and approvers along with the date and signature, where necessary. According to ICH E6 (2.12.2), "the investigator/institution should maintain adequate and accurate source records…	• Added reference outlining requirements to include traceability elements to ensure records are uniquely identifiable and accountable. • Updated reference to align with ICH GCP E6(R3)
	n/a	Pg. 4- The use of stamps in place of handwritten signatures is not permitted.	Clarified restriction of use of stamps in place of handwritten signatures.
	Pg. 3 - All individuals who generate/capture electronic clinical trial data (including data, findings, observations, and related documents) Pgs. 4-5 - 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… 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	All individuals who generate/capture electronic clinical trial data (including data, findings, observations, and related records) **C**ontemporaneous: All data must be recorded when it is generated and must always include handwritten or electronic signature/initials and date/time 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 records must not be pre-filled/completed… **O**riginal: 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 source or raw data. Original source records 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 records, DAIDS strongly advises against using these mediums to ensure clear,	Aligned terminology, guidance, and references with ICH GCP E6(R3) Clarified formats for signature requirements.

Source Records and Documentation Revision 01 (cont'd)	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.	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 records because they are not the first place the data was recorded.	
Source Records and Documentation Revision 01 (cont'd)	Pg. 5-6 - Complete: Data should be final, with no missing information or pages. The document must be complete until that point in time… 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… Certified Copy: As per ICH E6 (1.63): "A	**C**omplete: Data should be final, with no missing information or pages. The document must be complete by that point in time… Types of Source Records As discussed, a source record 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 records, but in this instance, the protocol should prospectively define which data may be treated in this way. As per ICH E6 (B.14.2; Clinical Trial Protocol), "The identification of data to be recorded directly into the data acquisition tools (i.e., no prior written or electronic record of data) and considered to be the source record." 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 records, and a few are defined here… Certified Copy: As per ICH E6 (Glossary): "A copy (irrespective of the type of media used) of	• Minor grammatical updates • Aligned terminology with ICH GCP E6(R3) • Updated ICH GCP E6(R3) references

Source Records and Documentation Revision 01 (cont'd)	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… Examples of electronic records include electronic medical records (EMRs)/electronic health records (EHRs), Microsoft (MS) Word/Excel documents… In these instances, the data must be printed, signed, and dated by the individual who	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, as the original, including relevant metadata, where applicable." 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 record would be acceptable. A certified copy must be signed or initialed and dated by the individual making the copy and containing 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 record 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 record… Examples of electronic records include electronic medical records (EMRs)/electronic health records (EHRs), Microsoft (MS) Word/Excel records… In these instances, the data must be printed, signed, and dated by the	• Minor grammatical updates • Aligned terminology with ICH GCP E6(R3) • Updated ICH GCP E6(R3) references

Source Records and Documentation Revision 01 (cont'd)	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. Pg. 7 - 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… Pg.8 - **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.	individual who electronically generated it. In this case, the paper is considered the source record and must not be discarded/replaced by a new printed, signed, and dated record. Any required updates to previously recorded data must be documented as a late entry. The appendix Source Records Requirements provides additional information about types of source records and requirements for generating data. The requirements for documentation, record-keeping, and record retention apply to all records. The SCORE manual's Essential Records section provides source record storage and retention requirements. **Error Correction** When generating data, errors in the original entry may occur and must be corrected as soon as they are identified… **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 records, document the deficiency and the circumstances surrounding the situation (if known). **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 records (source), including certified copies, even if they are updated through a late entry.	• Minor grammatical updates • Aligned terminology with ICH GCP E6(R3) • Updated ICH GCP E6(R3) references

Source Records and Documentation Revision 01 (cont'd)	Pg. 8 - **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"… Pg. 10 - 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. Pg. 9 - **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. When cases of incorrect or inconsistent data in a CRF occur, the data management center, contract	**Access to Source Records 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 (Glossary), 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 and may be performed on-site or remotely. 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 participants' identities and their data and sponsor's proprietary information". Never redact identifiers on original records, even if a new identifier is added to the record (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. Data reported to the sponsor should be identified by an unambiguous participant code that can be traced back to the identity of the participant by the investigator/institution. (ICH 2.12.8). **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 records. When cases of incorrect or inconsistent data in a CRF occur, the data management center,	• Minor grammatical updates • Aligned terminology with ICH GCP E6(R3) • Updated ICH GCP E6(R3) references

	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. Pg. 11 - **Appendices** 1. Source Records Requirements	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 record. **Appendices** 1. Source Records Requirements	
Appendix – Source Records Requirements Revision 02	Document Title - SCORE Manual: Appendix Source Documents Requirements Pg. 3 - **SOURCE DOCUMENTS** Source documents must follow the requirements detailed in the Source Documentation section of the DAIDS SCORE Manual. 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… 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	Document Title - SCORE Manual: Appendix Source Records Requirements **Source Records** Source records must follow the requirements detailed in the Source Records and Documentation section of the DAIDS SCORE Manual. Case Report Forms Used as Source Records Case report forms (CRFs) may be used as source records if data are 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 for 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 records… Note: Using CRFs as source records (direct and real-time entry) is different than using printed copies of electronic or paper CRFs as source records and then transcribing the data into the CRFs. If the CRS uses copies of CRFs (paper or electronic) as source records, 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 record worksheets or templates in the CRS procedures. Clear documentation for which CRFs are being used as source records should be readily	• Minor grammatical updates • Aligned terminology with ICH GCP E6(R3) • Updated ICH GCP E6(R3) references

Appendix – Source Records Requirements Revision 02 (cont'd)	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) Pg. 3-4 – 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. Pg. 6 – 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 Communications: Verbal… Signed and dated documentation that details actual or attempted communication with any of the following entities must be captured in the	available at the beginning of all monitoring visits. CRFs used as source records must also be maintained and available for review in the same manner as other source records. Common Deficiencies • Inadequately identifying who corrected a record 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 record 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 records, 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… Common Deficiencies • Missing participant identifiers (e.g., notes that exclude a participant's last name) may prevent attribution of the source record to the applicable participant Communications: Verbal… Signed and dated documentation that details actual or attempted communication with any of the following entities must be captured in	• Minor grammatical updates • Aligned terminology with ICH GCP E6(R3) • Updated ICH GCP E6(R3) references

Appendix – Source Records Requirements Revision 02 (cont'd)	research record, contact report, or other source document: Communications: Written… Forms of written communication may include documents such as admission/discharge summaries, letters, memoranda, and email correspondence. Pg. 5 – 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… 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… Common Deficiencies • Computer system used to record clinical research data (source document) does not meet the requirements necessary to ensure data quality and integrity. Pg. 5 – 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 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	the research record, contact report, or other source record: Communications: Written… Forms of written communication may include records such as admission/discharge summaries, letters, memoranda, and email correspondence. 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 record… CRS staff may use systems/software (e.g., email, MS Word/Excel) that lack user access controls, 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 record and must not be discarded/replaced by a new printed, signed, and dated record… Common Deficiencies • Computer system used to record clinical research data (source record) does not meet the requirements necessary to ensure data quality and integrity. Certified Copies According to ICH E6 (Glossary), 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 records are retained elsewhere at a CRS… • 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 record, as the external institution's medical chart cannot be retained at the CRS…	• Minor grammatical updates • Aligned terminology with ICH GCP E6(R3) • Updated ICH GCP E6(R3) references

Appendix – Source Records Requirements *Revision 02 (cont'd)*	external institution's medical chart cannot be retained at the CRS… • 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… • Documents that exceed one page may be verified in a package as a single certified copy if the package will remain intact when filed. Pg. 6 – Flow Sheets/Worksheets/Templates… 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 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… • CRFs, when used as source documents Pg. 8-9 – **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… **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	• Adding a signature/initials and date without a statement ▪ The dated signature/initials must reflect that the signatory has verified the record is an exact copy of the original per the CRS's standard operating procedures (SOPs) for creating certified copies… • Records that exceed one page may be verified in a package as a single certified copy if the package will remain intact when filed. Flow Sheets/Worksheets/Templates… Common Deficiencies • Leaving checkboxes unchecked on the record • Missing signature/initials and dates • Missing participant identifiers and dates • Inadequately identifying the individual responsible for each entry on a record that includes entries by multiple CRS staff Research Records… Research records constitute all records that substantiate data collected and/or are relevant to participants in a clinical trial. These may include… • CRFs, when used as source records **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 record data to support and ensure data integrity and participant safety… **Addenda (Addendum/Late Entry)** When source records 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	• Minor grammatical updates • Aligned terminology with ICH GCP E6(R3) • Updated ICH GCP E6(R3) references

Appendix – Source Records Requirements Revision 02 (cont'd)	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… 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… **CRS staff must NEVER modify previously dated source records in research documents if attempting to resolve deficiencies.** Altering, substituting, or discarding previously dated records is potentially fraudulent… 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. Pg. 10 - **Confidentiality…** 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). Pg. 11 – **Death…** If CRS staff is verbally notified of a participant´s death, they must record the following in the source document:	during a site visit. CRS staff can correct these records by recording an additional entry or addendum to the source record… When including an addendum to a source record, 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… **CRS staff must NEVER modify previously dated source records in research records if attempting to resolve deficiencies.** Altering, substituting, or discarding previously dated records is potentially fraudulent… In such situations, and others that may depart from norms, CRSs must include detailed records in the source record to ensure that anyone reviewing the documentation clearly understands the decision to deviate from the normal assent process. **Confidentiality…** Identifiers on original records must never be redacted, even if a new identifier is added to the record (e.g., placing a PID label over a participant's name or vice versa). **Death…** If CRS staff is verbally notified of a participant´s death, they must record the following in the source record: **Pg. 11 - Corrective and Preventive Actions (CAPA)** When protocol departures/deviations are identified, CRS staff should investigate the extent of the issue and, when applicable, implement corrective actions and appropriate measures to prevent recurrence. CAPAs must be documented to include root cause analysis and when pertinent, effectiveness checks.	• Minor grammatical updates • Aligned terminology with ICH GCP E6(R3) • Updated ICH GCP E6(R3) references • Added CAPA section to describe assessment of deviations/departures and consequent follow-up actions to address identified deficiencies identified.

Appendix – Source Records Requirements Revision 02 (cont'd)	Pg. 12 – **Entry Criteria (Inclusion/Exclusion Criteria)…** • Original documents or certified copies of protocol-required diagnostic results and/or medical history (e.g., laboratory results, radiology report, medication history, etc.). Pg. 12-13 – **Identifiers** CRSs must consistently label all source documents with at least one unique identifier so anyone can verify that records correspond to a particular participant. Unique identifiers include a participant's:… 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… In addition, consenters must assess whether participants/their LARs understand the information presented in the ICF and document their assessment in the source documents. Pg. 15 – **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	**Entry Criteria (Inclusion/Exclusion Criteria)…** • Original records or certified copies of protocol-required diagnostic results and/or medical history (e.g., laboratory results, radiology report, medication history, etc.). **Identifiers** CRSs must consistently label all source records with at least one unique identifier so anyone can verify that records correspond to a particular participant. Unique identifiers include participant:… NEVER obliterate identifiers on original records, even if a new identifier is added to the record (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 records on site… In addition, consenters must assess whether participants/their LARs understand the information presented in the ICF and document their assessment in the source records. **Procedures: Diagnostic, Therapeutic, Surgical and others.** If CRS staff request any procedures be conducted on a participant, it must be accompanied by 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	• Minor grammatical updates • Aligned terminology with ICH GCP E6(R3) • Updated ICH GCP E6(R3) references

Appendix – Source Records Requirements Revision 02 (cont'd)	diagnostic procedures in the source document, whether required by the protocol or not. Pg. 16 - **Questionnaires: Completed by Participant/LAR and/or Study Personnel…** *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…* Completed questionnaires are considered source documents and must always be retained as part of participant charts/research records.	procedures in the source record, whether required by the protocol or not. **Questionnaires: Completed by Participant/LAR and/or Study Personnel…** *Note: if a protocol requires CRS staff to remain blinded to information on completed questionnaires the record must be returned to the unblinded study staff to be stored securely…* Completed questionnaires are considered source records and must always be retained as part of participant charts/research records.	
	Pg. 17 - Toxicities: Grading (AEs, Signs and Symptoms, Laboratory Results) ~~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.~~	**Toxicities: Grading (AEs, Signs and Symptoms, Laboratory Results)** CRS staff are required to document and grade all AEs in participant research records to determine reportability of the AEs.	• Clarified requirements for assessment, documentation and reporting of AEs.
Essential Records Revision 01	Document Title – Essential Records Pg. 2 - **Essential Documents** Essential documents, individually and collectively, serve to demonstrate Principal Investigator (PI)/Investigator of Record (IoR), DAIDS, and monitoring contractor compliance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) requirements ("ICH E6") and any applicable local laws and regulations .	Document Title – Essential Documents **Essential Records** Essential records, individually and collectively, serve to demonstrate Principal Investigator (PI)/Investigator of Record (IoR), DAIDS, and monitoring contractor compliance with International Council for Harmonisation (ICH) Good Clinical Practice (GCP) requirements ("ICH E6") and any applicable local laws and regulations. Good Documentation Practices must also be followed for Essential Records (see Source Records and Documentation section where details are outlined).	• Aligned terminology based on ICH GCP E6(R3). • Added reference to GDP standards applicable to Essential Records

Essential Records *Revision 01* *(cont'd)*	Pg. 2 - **Recordkeeping and Retention Requirements for Essential Documents** Essential documents include a variety of documents as described in Section 8 and section 4 of the ICH E6 guidelines and additional documents required by DAIDS… Please refer to Essential Documents Recordkeeping appendix of this section for additional guidance.	**Recordkeeping and Retention Requirements for Essential Records** Essential records include a variety of records as described in Section 8 of the ICH E6 guidelines and additional records required by DAIDS… Please refer to Recordkeeping for Essential Records appendix of this section for additional guidance.	
		Pg. 5 - Requirements for Storing Clinical Research Records CRS staff must store CRRs in a manner that keeps files private, confidential, secure, and accessible (to appropriate parties) throughout the clinical trial and after it concludes. CRRs may be kept in hard copy, electronic, or other media format. CRS staff should maintain a record of where essential records are located, including source records. The storage system(s) used during the trial and for archiving (irrespective of the type of media used) should provide for appropriate identification, version history, search and retrieval of trial records.	• Added recommendations for systems for organizing essential records
	Pg. 6 - **Requirements for Retaining Clinical Research Records…** Under the terms of the Grant Award, CRRs are the property of the awardee institution. U.S. Department of Health and Human Services 45 Code of Federal Regulations (CFR) Part 46.115(b) requires research records to be retained for at least three [3] years after completion of the research, as well as, be retained in compliance with ICH E6. Electronic data must be stored in a format that will be accessible and readable for years to come.	**Requirements for Retaining Clinical Research Records…** Under the terms of the Grant Award, CRRs are the property of the awardee institution. U.S. Department of Health and Human Services 45 Code of Federal Regulations (CFR) Part 46.115(b) requires research records to be retained for at least three [3] years after completion of the research, as well as, be retained in compliance with ICH E6, any applicable regulatory requirements or until the sponsor informs the investigator/institution that these records are no longer needed, whichever is the longer.	• Added clarification that other regulatory agency and sponsor requirements may apply to record retention timeframe.
		DAIDS Trial Master File For registrational studies, which are conducted with the purpose of submitting trial data for review by regulatory agencies for marketing approval, DAIDS may implement a Sponsor Trial Master File (TMF). The Sponsor TMF contains	• Added section related to DAIDS TMF outlining sponssor and investigator responsibiltiy for maintenance of the TMF and associated essential records.

		the essential records and clinical research records that individually and collectively permit the evaluation of the trial's conduct and data quality. DAIDS utilizes a decentralized approach for TMFs, where TMF records are not stored solely at DAIDS, but are retained in multiple DAIDS-approved electronic systems or other locations. The essential records generated and retained at the CRS make up part of the DAIDS Sponsor TMF. These site-generated essential records generally remain at the site for the duration of the trial and the required record retention period. However, these records could be required to be brought into the Sponsor TMF, for example in preparation for a sponsor inspection, or at the request of a pharmaceutical company for a marketing application. The Investigator/Institution is responsible for adequately maintaining these records at the site (in either paper or electronic format), in accordance with DAIDS-OPC-A15-POL00015 Storage and Retention of Clinical Research Records Policy. In instances where an investigator / institution is unable to retain their records for the required retention time period, studies with a DAIDS Sponsored TMF will be identified to ensure all site-generated essential records that are part of the TMF are maintained per the retention processes listed below. **Retention Time Periods Applicable to DAIDS Sponsor Records at the CRS** For site records that are part of a DAIDS Sponsor TMF, the CRS must ensure that these TMF records are maintained for the retention time period applicable to the entire TMF. The CRS should contact their DAIDS OCSO PO if there are questions about which DAIDS studies have a Sponsor TMF. • In circumstances where multiple sets of requirements apply, the most stringent applicable retention requirement must be followed. These additional requirements include national, state, and local	• Added section Retention Time Periods Applicated to DAIDS Sponsor Records at the CRS outlining requirements for record retention timeframes for TMF essential records. This section also provides guidance for sites requiring additional assistance with transfer of TMF records.

		laws as well as institutional policies which may extend the record retention requirement. It is the Site Investigator's responsibility to know and/or to confirm the national/local/institutional record retention requirements that pertain to their site. • According to ICH, when data from a study was used as part of a marketing application, the sponsor and investigator/site shall retain research study records for an amount of time following the defined milestone (e.g., the end of the clinical trial, final approval of application, discontinuation of clinical development of the investigational product, etc.). o If data were used in a marketing application submitted to the EMA, records must be retained for at least 25 years from the end of the clinical trial. o If data were used in a marketing application submitted to the FDA, records must be retained for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated. o If data were used in a marketing application submitted to the EMA and FDA, records must be retained for at least 25 years from the end of the clinical trial (the more stringent retention requirements apply). o If the Site Investigator does not know if data	

		were used to support a marketing application, DAIDS should be contacted to confirm the record retention requirements. The CRS should follow all requirements for source documentation/essential records, including for records that are part of the DAIDS Sponsor TMF. These include details outlined in the requirements below. • DAIDS SCORE Manual - Source Records and Documentation section • DAIDS Electronic Information Systems (EIS) policy • DAIDS Policy on Storage and Retention of Clinical Research Records (DAIDS-OPC-A15-POL-00015) includes specific processes, locations, and CRS records which must be retained or migrated. In the event the CRS cannot retain their TMF records for the required Sponsor TMF record retention period, DAIDS will accept CRFs, pharmacy records and additional clinical research site records required by the Sponsor TMF. The CRS should discuss with their DAIDS OCSO PO who will work with the DAIDS TMF Team on record transfer. Sites may also reference the RSC website for guidance: DAIDS Storage and Retention of Clinical Research Records.	
Recordkeeping for Essential Records Revision 01 *Recordkeeping for Essential Records* *Revision 01 (cont'd)*	Pg. 1 - Document Title**: Essential Documents Recordkeeping** This appendix provides a detailed list of essential documents. The purpose and/or description of these documents is/are given with a recommended location where they should be filed during the conduct of a clinical trial.	**Document Title: Recordkeeping for Essential Records** This appendix provides a detailed list of essential documents. This is not an exhaustive list. Other trial records may be considered essential by the sponsor, or applicable local regulations or requirements (per ICH GCP E6(R3) Appendix C3.3). The purpose and/or description of these documents is/are given with a recommended location where they should be filed during the conduct of a clinical trial.	• Aligned terminology and guidances based on ICH GCP E6(R3). • Added clarification regarding the scope of essential records. • Clarified formats for different CRFs.

	Pg. 1 – **Case Report Form (CRF)** Form designed to capture all protocol required information that must be reported to DAIDS on each clinical trial participant. ~~• CRFs can be paper or electronic CRF (eCRF) format.~~	**Case Report Form (CRF)** Form (printed, optical, or electronic) designed to capture all protocol required information that must be reported to DAIDS on each clinical trial participant.	• Clarified formats for CRFs
	Pg. 3 – **Documentation of Equipment Calibration and/or Maintenance** Documentation of the calibration and/or maintenance of equipment used throughout the clinical trial	**Documentation of Equipment Calibration and/or Maintenance** Maintenance and calibration records for critical trial-specific equipment.	
	Pg. 12 – **Site Monitoring Reports** Monitoring contractor reports that document: • Site monitoring visits • Monitor findings • Review of clinical trial procedures with the PI/IoR and site staff	**Site Monitoring and Other Reports (including site selection, initiation, route and close-out)** Reports that document: Site monitoring visits Monitor findings Review of clinical trial procedures with the PI/IoR and site staff Site assessment Protocol initiation Site Closeout (if applicable)	• Added additional types of monitoring visits
	Pg. 13 - ~~**Initiation Monitoring Report**~~ ~~To document that clinical trial procedures were reviewed with the PI/IoR and their clinical trial staff. This may be combined with a pre-trial monitoring report and documented as a training when a site initiation visit does not apply.~~	n/a	• Deleted section and incorporated into **Site Monitoring and Other Reports** section
	Pg. 14 – **Source Documents** ~~Electronic media, original documents, or certified copies that document the existence of the participant and substantiate collected clinical trial data integrity. This includes documents related to the clinical trial, medical treatment, participant history, and participant's condition while on study or in follow-up.~~ ~~Refer to the SCORE Manual's Source Documentation section for additional requirements.~~	**Source Records** Original documents or data (which includes relevant metadata) or certified copies of the original documents or data, irrespective of the media used. This may include trial participants' medical/health records/notes/charts; data provided/entered by trial participants (e.g., electronic patient-reported outcome (ePROs)); healthcare providers' records from pharmacies, laboratories and other facilities involved in the clinical trial; and data from automated instruments, such as wearables and sensors. Refer to the SCORE Manual's Source Records and Documentation section for additional requirements.	• Expanded definition of Source Records based on updated guidance from ICH GCP E6(R3). • Added section to provide guidance of

	n/a	**Systems Validation** Documentation of systems specifications, testing, validation, and change control.	documentation requirements for Electronic systems used at site
Quality Management Revision 01	Pg. 3 - CRSs must file all current and obsolete SOP versions according to DAIDS clinical research records storage and retention requirements described in Essential Documents section of the SCORE Manual. b. Determine Key Indicators (KIs) for QA/QC review, including:… b. Source Documents, Signatures, Initials, Dates	CRSs must file all current and obsolete SOP versions according to DAIDS clinical research records storage and retention requirements described in Essential Records section of the SCORE Manual. b. Determine Key Indicators (KIs) for QA/QC review, including:… • Source Records, Signatures, Initials, Dates	• Updated reference to align with ICH GCP E6(R3) terminology
Informed Consent of Participants Revision 02	Pg. 6-7 - Before any study-specific procedures (including screening) are conducted: • Assess whether participants understood the ICF information presented to them, document this assessment of understanding in the source documents… • Provide a copy of the signed ICF as per local requirements/SOP to participants and document in the source documents that the ICF (original or copy) was offered to the participants. The person obtaining consent must also note (in the source documents) cases where participants refuse to take the signed ICF copy. • Review the signed ICF and its documentation in the source documents to ensure the person obtaining informed consent administered a proper consent process to the participant. Pg. 9 – **Minors in Clinical Research…** In those cases, CRSs must include adequate documentation to support the lack of assent in the source documents and inform the IRB/EC, if applicable.	Before any study-specific procedures (including screening) are conducted: • Assess whether participants understood the ICF information presented to them, document this assessment of understanding in the source records… • Provide a copy of the signed ICF as per local requirements/SOP to participants and document in the source records that the ICF (original or copy) was offered to the participants. The person obtaining consent must also note (in the source records) cases where participants refuse to take the signed ICF copy. • Review the signed ICF and its documentation in the source records to ensure the person obtaining informed consent administered a proper consent process to the participant. **Minors in Clinical Research…** In those cases, CRSs must include adequate documentation to support the lack of assent in the source records and inform the IRB/EC, if applicable.	• Aligned terminology with ICH GCP E6(R3)

Appendix – CRS Requirements for Enrolling Minors into DAIDS Clinical Research Revision 02	Pg. 2 – **Institutional Review Board/Ethics Committee Risk Benefits Assessment…** • Written determination of the risk/benefit category from the IRB/EC is maintained in the essential documents file.	**Institutional Review Board/Ethics Committee Risk Benefits Assessment…** • Written determination of the risk/benefit category from the IRB/EC is maintained in the essential records file.	• Aligned terminology with ICH GCP E6(R3)
Screening, Enrollment, Randomization, and Unblinding of Participants Revision 01	Pg. 4 – **Age and Identity Verification** Each CRS should seek the approval of their local Institutional Review Board (IRB)/ Ethics Committee (EC) before implementing the SOP. Pg. 7 – **Unblinding Participants' Treatment** ICH E6 Section 4.7 states: "The investigator should follow the trial's randomization procedures, if any, and should ensure that the code is broken only in accordance with the protocol. ~~If the trial is blinded~~, the investigator should promptly document and explain to the sponsor any premature unblinding (e.g., accidental unblinding, unblinding due to a ~~serious adverse event~~) of the investigational product(s)".	**Age and Identity Verification** Each CRS must seek the approval of their local Institutional Review Board (IRB)/ Ethics Committee (EC) before implementing the SOP…. Each CRS must be knowledgeable about local requirements for the protection of personal data. It is the site's responsibility to ensure that an Informed Consent Form is in place before collecting participants' personal information. It is also recommended that site SOPs clearly describe the steps required to obtain such information. **Unblinding Participants' Treatment** ICH E6 Section 2.11 states: "The investigator should follow the trial's randomization procedures, if any, and, in the case of an investigator-blinded trial, should ensure that the code is broken only in accordance with the protocol. In the case of an emergency, to protect patient safety, the investigator should be prepared and capable from the start of the trial to perform unblinding without undue delay and hinderance. The investigator should promptly document and explain to the sponsor any premature unblinding (e.g., accidental unblinding, emergency unblinding to protect trial participant, unblinding due to an SAE) of the investigational product(s)".	• Aligned language to reflect requirement • Added language to clarify CRS responsibility to maintain awareness and compliance with local regulations pertaining to • Updated reference based on ICH GCP E6(R3).

Site Visits Revision 01	Pg. 2 – **Site Visits** According to the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guidelines "ICH E6" (5.18.3): "Extent and Nature of Monitoring: The sponsor should ensure that the trials are adequately monitored. The sponsor should determine the appropriate extent and nature of monitoring. The determination of the extent and nature of monitoring should be based on considerations such as the objective, purpose, design, complexity, blinding, size, and endpoints of the trial. In general, there is a need for on-site monitoring, before, during, and after the trial." To fulfill the regulatory oversight obligation, DAIDS (as sponsor) delegates monitoring responsibility to a Monitoring Contractor (Contract Research Organization --CRO), which in turn assigns monitors (also known as Clinical Research Associates – CRAs) to conduct the visits. ICH E6 (5.0) – Quality Management "requires that the sponsor implement a system to manage quality throughout all stages of the study process" and use a risk-based approach… Monitors, auditors, and inspectors are typically unblinded and can have access to these documents. Pg. 3 - CRSs must prepare for the visit, ensuring that:… • Copies of requested documents are ready for the monitor at the start of the visit (e.g., Delegation of Duties log, documentation reflecting PI/IoR involvement in the study, Form FDA 1572, etc.). Pg. 5 – **Interim Site Monitoring Visit** Interim Site Monitoring Visits (ISMVs) evaluate the conduct of the study by performing source document and other verifications…The ISMV can also be performed remotely at the request of DAIDS and the usual purpose is to review regulatory documents and EDC data.	**Site Visits** According to the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guidelines "ICH E6" (34): "The sponsor should determine the appropriate extent and nature of monitoring, based on identified risks." To fulfill the regulatory oversight obligation, DAIDS (as sponsor) delegates monitoring responsibility to a Monitoring Contractor (Contract Research Organization --CRO), which in turn assigns monitors (also known as Clinical Research Associates – CRAs) to conduct the visits. ICH E6 (3) – Quality Management "requires that the sponsor should implement an appropriate system to manage quality throughout all stages of the trial process" and use a risk-based approach… Monitors, auditors, and inspectors are typically unblinded and can have access to these records. CRSs must prepare for the visit, ensuring that:… • Copies of requested records are ready for the monitor at the start of the visit (e.g., Delegation of Duties log, documentation reflecting PI/IoR involvement in the study, Form FDA 1572, etc.). **Interim Site Monitoring Visit** Interim Site Monitoring Visits (ISMVs) evaluate the conduct of the study by performing source record and other verifications…The ISMV can also be performed remotely at the request of DAIDS and the usual purpose is to review regulatory records and EDC data.	• Aligned with terminology and references in ICH GCP E6(R3). • Aligned with terminology and references in ICH GCP E6(R3).

Site Visits Revision 01 (cont'd)	Pg. 6 – ***Pharmacy Assessment*** The PSIDA includes at least the following: • Assessment of investigational pharmacy personnel • Verification of pharmacy records ~~and records,~~ including dispensation and preparation documentation Pg. 8 – **CRS Closeout** The overall site closeout proceeds according to DAIDS instructions/direction, verifying that:… • All essential documents have been stored or transferred, including but not limited to the following: ▪ Source documents (original research records, clinic notes, and hospital notes) ▪ IRB/EC and regulatory submissions and approvals ▪ Protocols and related documents, such as amendments ▪ Paper CRFs (if applicable) **Note:** When local and/or institutional requirements exceed these storage/retention requirements, the local/institutional requirements must be followed. Please refer to the Essential Documents section of this manual for more information on retention of records. Pg. 9 - **Quality Management Audits** According to ~~ICH E6 5.19.1~~: "The purpose of a sponsor's audit, which is independent of, and separate from routine monitoring or quality control functions, should be to evaluate trial conduct and compliance with the protocol, Standard Operating Procedures (SOPs), GCP, and the applicable regulatory requirements." DAIDS Quality Management is responsible for the conduct of all site audits… **Note:** Related records, such as the audit report and audit responses document (CAPA), are **not** to be maintained in the study-specific files. As per ~~ICH E6 5.19.3(d)~~: "To preserve the independence and value of the audit function, the regulatory authority(ies) should not routinely	***Pharmacy Assessment*** The PSIDA includes at least the following: • Assessment of investigational pharmacy personnel • Verification of pharmacy records including dispensation and preparation documentation **CRS Closeout** The overall site closeout proceeds according to DAIDS instructions/direction, verifying that:… • All essential records have been stored or transferred, including but not limited to the following: ▪ Source records (original research records, clinic notes, and hospital notes) ▪ IRB/EC and regulatory submissions and approvals ▪ Protocols and related records, such as amendments ▪ Paper CRFs (if applicable) **Note:** When local and/or institutional requirements exceed these storage/retention requirements, the local/institutional requirements must be followed. Please refer to the Essential Records section of this manual for more information on retention of records. **Quality Management Audits** According to ICH E6 3: "The purpose of a sponsor's audit, which is independent of and separate from routine monitoring or quality control functions, is to evaluate whether the processes put in place to manage and conduct the trial are effective and compliant…" Audits are intended to prepare for and evaluate site inspection readiness… **Note:** Related records, such as the audit report and audit responses document (CAPA), are **not** to be maintained in the study-specific files. As per ICH E6 3.11.2.2(d): "To preserve the independence and value of the audit function, the regulatory authority(ies) should not	Aligned with terminology and references in ICH GCP E6(R3).

Site Visits *Revision 01 (cont'd)*	request the audit reports. Regulatory authority(ies) may seek access to an audit report on a case-by-case basis when evidence of serious GCP non-compliance exists, or in the course of legal proceedings." Therefore, it is recommended that the CRS maintains such documents in a separate file. Pg. 10-11 - **Routine Investigator Site Audit** Routine Investigator Site Audits are the most common type conducted as part of DAIDS' quality management program. They assess the study conduct and compliance with the study protocol, procedural documents, GCP, DAIDS' and other applicable regulatory requirements. **For-Cause Investigator Site Audit** For-Cause Investigator Site Audits investigate reported serious and/or persistent noncompliance with the study protocol, procedural documents, GCP, applicable regulatory requirements, and/or DAIDS directives. They can also happen when scientific misconduct (e.g., fabrication and/or falsification of data) is suspected. **Site Inspection Readiness Visit (SIRV)** Site Inspection Readiness Visits prepare CRS for Regulatory Authority inspections. Preparation is investigator-centric and may be either on-site or remote. On-site visits may include an educational presentation, high-level review to verify the presence of study documents…	routinely request the audit reports. Regulatory authority(ies) may seek access to an audit report on a case-by-case basis when evidence of serious GCP non-compliance exists, or in the course of legal proceedings." Therefore, it is recommended that the CRS maintains such records in a separate file. **Routine Investigator Site Audit** Routine Investigator Site Audits are the most common type conducted as part of DAIDS' quality management program. They assess the study conduct and compliance with the study protocol, procedural records, GCP, DAIDS' and other applicable regulatory requirements. **For-Cause Investigator Site Audit** For-Cause Investigator Site Audits investigate reported serious and/or persistent noncompliance with the study protocol, procedural records, GCP, applicable regulatory requirements, and/or DAIDS directives. They can also happen when scientific misconduct (e.g., fabrication and/or falsification of data) is suspected. **Site Inspection Readiness Visit (SIRV)** Site Inspection Readiness Visits prepare CRS for Regulatory Authority inspections. Preparation is investigator-centric and may be either on-site or remote. On-site visits may include an educational presentation, high-level review to verify the presence of study records…	Aligned with terminology and references in ICH GCP E6(R3).

Clinical Research Site Inspection Readiness Revision 01	Pg. 3-4 - Additional guidance on GDP and CQMP is provided in the DLP, DAIDS Clinical Trials Networks Study Specific Procedures, Manual of Operations/Procedures and in the Source Documentation and Quality Management sections of this manual. Some of the essential documents that a CRS is to include in their regulatory files are: • Executed (signed) informed consent form(s) (ICFs) for all participants • Study source documents and participants' research records, as applicable For a complete list of essential documents, refer to the Essential Documents Recordkeeping appendix in the Essential Documents section of this manual. Pg. 9 - **CR (Critical):** The inspector(s) identified conditions, practices, or processes adversely affecting the rights, safety, or well-being of the participants and/or the quality and integrity of data. Critical observations may include a pattern of deviations classified as: major, poor quality of the data, and/or absence of source documents. Manipulation and intentional misrepresentation of the data would be classified as critical.	Additional guidance on GDP and CQMP is provided in the DLP, DAIDS Clinical Trials Networks Study Specific Procedures, Manual of Operations/Procedures and in the Source Records and Documentation and Quality Management sections of this manual. Some of the essential records that a CRS is to include in their regulatory files are: • Executed (signed) informed consent form(s) (ICFs) for all participants • Study source records and participants' research records, as applicable… For a complete list of essential records, refer to the Recordkeeping for Essential Records appendix in the Essential Records section of this manual. • **CR (Critical):** The inspector(s) identified conditions, practices, or processes adversely affecting the rights, safety, or well-being of the participants and/or the quality and integrity of data. Critical observations may include a pattern of deviations classified as: major, poor quality of the data, and/or absence of source records. Manipulation and intentional misrepresentation of the data would be classified as critical.	Aligned with terminology and references in ICH GCP E6(R3). Aligned with terminology and references in ICH GCP E6(R3).
Appendix – Guidance on Site Regulatory Inspection Revision 02	Pg. 3 – **Logs and Documents Provided to the Inspector** • Create a shadow file of documents copied and keep a copy at the site. Pg. 4 - **Data Inspectional triggers include: …** • Post-it notes left on source documents, not part of participant data • Unsigned or late review of laboratory reports, Adverse Events or Serious Adverse Events • Unauthorized changes to clinical trial documents including persons not listed	**Logs and Records Provided to the Inspector** • Create a shadow file of records copied and keep a copy at the site. **Data Inspectional triggers include: …** • Post-it notes left on source records, not part of participant data • Unsigned or late review of laboratory reports, Adverse Events or Serious Adverse Events • Unauthorized changes to clinical trial records including persons not listed on the	Aligned with terminology and references in ICH GCP E6(R3).

	on the Delegation of Duties Log or not having the appropriate credentials or training	Delegation of Duties Log or not having the appropriate credentials or training	