

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

Guidance on Site Regulatory Inspection

This document provides additional guidance to follow before, during, and after a regulatory inspection, as well as some triggers for inspections at sites.

Notification of an Inspection

Notify DAIDS Office of Clinical Site Oversight (OCSO) Program Officer (PO), Contract Research Organization (CRO) (if applicable), and other stakeholders of inspection dates within **one business day for scheduled inspections** and as soon as possible for “for-cause” inspections.

Before the Inspection

Prepare in advance for scheduled inspections. If possible, change schedules for Clinical Research Site (CRS) staff and participant visits to accommodate the inspection when possible. Participant visits should, however, NOT take place outside of the window permitted by the protocol.

Point of Contact

Someone should be designated as the Point of Contact (POC) for the inspection at the CRS. This individual must:

- Be cognizant of all CRS activities relating to the clinical trial being inspected and whom to contact for each functional area.
- Accompany the inspector at all times.
- Speak English. Even if the inspector speaks Spanish, Thai, or Portuguese, the POC must be able to communicate effectively in English.

Tips for Handling Communication During the Inspection

- Notify the CRS staff when the inspector is on site and advise them to be available throughout the inspection.
- Inform CRS staff that they will receive a phone call if/when they are needed.
- Limit communications related to inspection activities to phone calls and minimize emails as they create a record.
- POC should provide a debrief to the Principal Investigator/Investigator of Record (PI/IoR) at the end of each day.
- POC may also hold a daily debriefing with CRS staff after once the inspector leaves. However, avoid putting such communications in writing, as we do not want to create a record based on a conversation.

Tips for Inspector Interviews with Clinical Research Site Staff

- CRS staff should be at the site 30 minutes before the inspector's planned arrival time. This allows members to compose themselves and prepare for their interviews.
- In a large clinical trial, it is likely that the inspector will ask to speak with key staff members. The POC should set up these staff interviews, if the inspector requests.
- If the inspector asks to speak with someone, that individual must become available with a reasonable amount of time (within one to two hours). It is acceptable to tell the inspector that the individual is not currently available but will be shortly.
- POC (or designee) should/must remain with the inspector while they are interviewing other site staff.
- Assign a staff member to take notes during each staff interview to document the question asked and the answer given.
- Always provide a translator if necessary. If the POC cannot serve as translator during an interview, appoint someone who can.

One person from each functional area such as pharmacy or laboratory should be responsible for responding to questions about that area to avoid giving contradictory responses. Most successful interviews are restricted to the individual who is most knowledgeable about the questions being asked.

Tips for Answering Questions Directly

- Answer questions without providing extraneous information.
- **Listen** to the question and don't be afraid to ask the inspector to repeat it if you do not understand.
- Answer only the question that is asked. Do not provide any additional background or information unless the inspector specifically asks for more. Providing more information than is needed may lead the inspector to ask more questions which may prolong or complicate the inspection. If the inspector is not satisfied with the response, they will ask another question.
- Only speak to topics that you are responsible for, do not speculate or guess on topics outside of your area of expertise.

Note: There may be an uncomfortable silence after you respond to the inspector, and that is fine. Practicing role playing can help CRS staff get comfortable with moments of silence that may occur following a response to an investigator's question.

Tips for Etiquette: Do's and Don'ts

- Stay focused and only give the inspector what they ask for.
- Do not attempt to recognize or showcase staff during the inspection.
- Do not have a group of staff meet with the inspector or accompany them on a tour of the site.
- Maintain a friendly cooperative environment but be mindful that this is a formal inspection and not a monitoring visit.
- Do not allow the inspector to freely move about the CRS at any time.

- Do not purchase food for the inspector but do facilitate provision of food.
- Do offer refreshments, like water, tea.
- Do not sign or make corrections to affidavits (written statements).
- Do not offer any type of gifts.
- Do not offer the inspector a ride back to their hotel but do offer to call a taxi or otherwise help facilitate their transportation.

We understand the desire to be hospitable. And transportation may especially be necessary at some locations, when there are security/safety issues. However, it is not advisable for CRS staff to accompany the inspector in a vehicle, as this affords an opportunity of further questioning for which CRS staff may be unprepared and/or should not address.

Research Records from Other Studies

Please note that an inspector may ask to look at participant research records of another study. While this is permissible, they should state the reason, however, for wanting to review another study's records.

Logs and Records Provided to the Inspector

- Maintain a log of copied documents, recording the order in which they were requested by the inspector.
- Create a shadow file of documents copied and keep a copy at the site.

Requests for Computers, Passwords, Database Access

CRS staff must keep all passwords (electronic Case Report Forms (CRF), database, or Electronic Medical Record [EMR] access) as well as personal access codes secure and never share these with an inspector. If the inspector requests to see the database or EMRs, the CRS staff must access the system on behalf of the inspector and remain with the inspector at all times during access.

It is acceptable to allow access to the internet on a laptop. Although inspectors may request computers for all of their team and access to the data, let them know they could use a laptop to access the internet; and ideally, inspector(s) would bring their own laptops.

Regarding the Inspection's Outcome

DAIDS will not receive information about the inspection's outcome. The PI/IoR will receive a copy of the inspection report and should immediately forward it by e-mail to the OCSO PO.

Data, Laboratory and Pharmacy Inspectional Triggers

Listed below is some helpful information showing what can cause inspectors to focus on data, laboratory and pharmacy issues during an inspection.

Data Inspectional triggers include:

- Data that is too perfect – no mistakes or cross-outs; re-copied or transcribed data
- No variance in the data. For example, all of the participants have the same blood pressure measurements or the same height.
- Data that does not make sense, e.g., unexplained height or weight changes
- Data where the number of missing values/dropouts does not meet the reviewer's expectation for the active substance or the type of measurement
- Progress notes out of order/late entries squeezed in
- Handwriting/signature irregularities
- Missing participant research records or unexplained gaps in the participant research records
- 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 Delegation of Duties Log or not having the appropriate credentials or training
- Too many deviations or too many notes to file
- Obscuring original data entry (white-out, scratch-out or obliteration of original entry)
- Using the CRF as source inappropriately
- Approved Exemptions to the protocol

Laboratory Inspectional Triggers that inspectors focus on include:

- Inconsistencies between the numbers of samples collected, analyzed and reported
- Insufficient information to confirm the integrity of the samples (e.g., regarding storage, shipment and stability)
- Management of repeat sample analyses and missing samples is not described adequately
- Timing for obtaining samples
- Large number of samples for re-assay

Pharmacy inspectional triggers that inspectors focus on include:

- Unsupervised Pharmacy technicians performing pharmacist responsibilities
- Study product and commercial medication stored on shelves that are not properly labeled
- Failure to maintain an adequate pharmacy inventory
- Inadequate security measures (cameras, alarms, key card, and key or computer access)
- No documentation to show controlled access to pharmacy (e.g., individuals other than pharmacist have a key to pharmacy area)
- Pharmacist not on study has access to study product
- Food or other non-medications (e.g., laboratory samples) being stored in refrigerator with medications (applies to general inspection of pharmacy area)
- Documentation that does not appear to reflect real-time entries

- Process errors documented that relate back to failure to follow pharmacy process for receipt, storage, return, study product accountability discrepancies and destruction of study product
- Missing information or documentation that is not current for the period of the clinical trial, such as:
 - Signed curricula vitae of pharmacist(s) or key pharmacy personnel
 - Prescriptions and administration of study products
 - Documentation of protocol training
 - Licenses of pharmacy personnel
 - Signature list and/or Delegation log
 - Study Product accountability logs (e.g., not all records are present, not all discrepancies verified)
 - Current approved version of the protocol and/or all of the approved versions
 - Records of study product dispensation to delegated CRS staff or not all records present
 - Temperature logs for all protocol-required equipment (e.g., refrigerator, freezers, storage cabinets)
 - Calibration and maintenance records
 - Current version of Investigator's Brochure(s) or Package Insert(s)
 - Certificates of analysis of investigational product shipped; all must be present, including new batches
 - Instructions for handling study product and clinical trial-related material to confirm inspection and integrity of the study product and trial-related material (e.g., regarding inspection, storage, shipment and stability, and destruction)

E-learning Available

Additional information and guidance relating to regulatory inspection preparedness are available through training modules offered on the DAIDS Learning Portal (DLP).

Revision Summary

Version/ Revision	Summary of Changes
1.0	Original version; became effective on 1/19/2021
01	DAIDS-OCS-A28-MAN-00028 rev 01 is the first revision of this manual in MasterControl. The document numbering and document format have been updated to reflect current requirements Version became effective on 8/15/2025.
02	DAIDS-OCS-A28-MAN-00028 rev 02 is a revision to align terminology with ICH GCP E6(R3).