



Audit Findings – Avoiding Pitfalls in Source Documentation

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Learning Objectives

- *Define source document*
- *Discuss the importance of source documentation*
- *Learn methods to ensure good source documentation practice*
- *Understand good practices of using the Electronic Health Record (EHR) in clinical research documentation*
- *Familiarize yourself with FDA regulations on electronic signatures and storage*

Source Data

“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.”

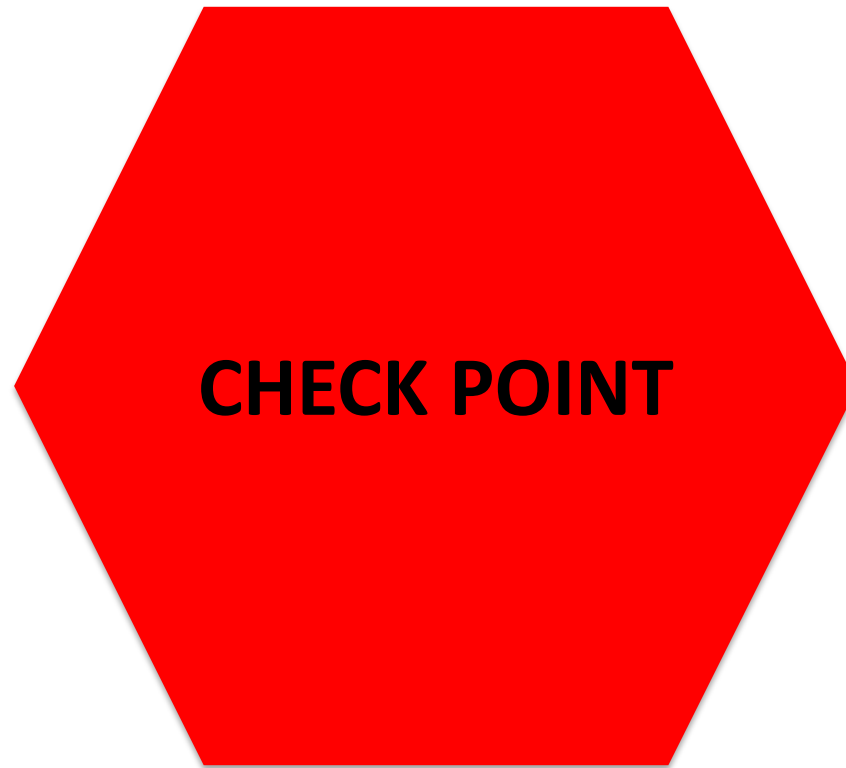
Source Documents

Original documents, data, and records such as:

- Hospital records
- Clinic and office charts
- Laboratory notes
- Subject diaries
- Procedural reports (EKGs, testing results, etc)
- Media (X-rays, photographs, videos, etc.)
- Records kept at pharmacy

Case Report Forms (CRFs)

“A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject.”



A coordinator forgets to bring a CRF in the participant's room, and writes the participant's vitals on a sticky note. The vitals are later transferred to the CRF, and the sticky note is thrown away. What is the source document?

Why is source documentation important?



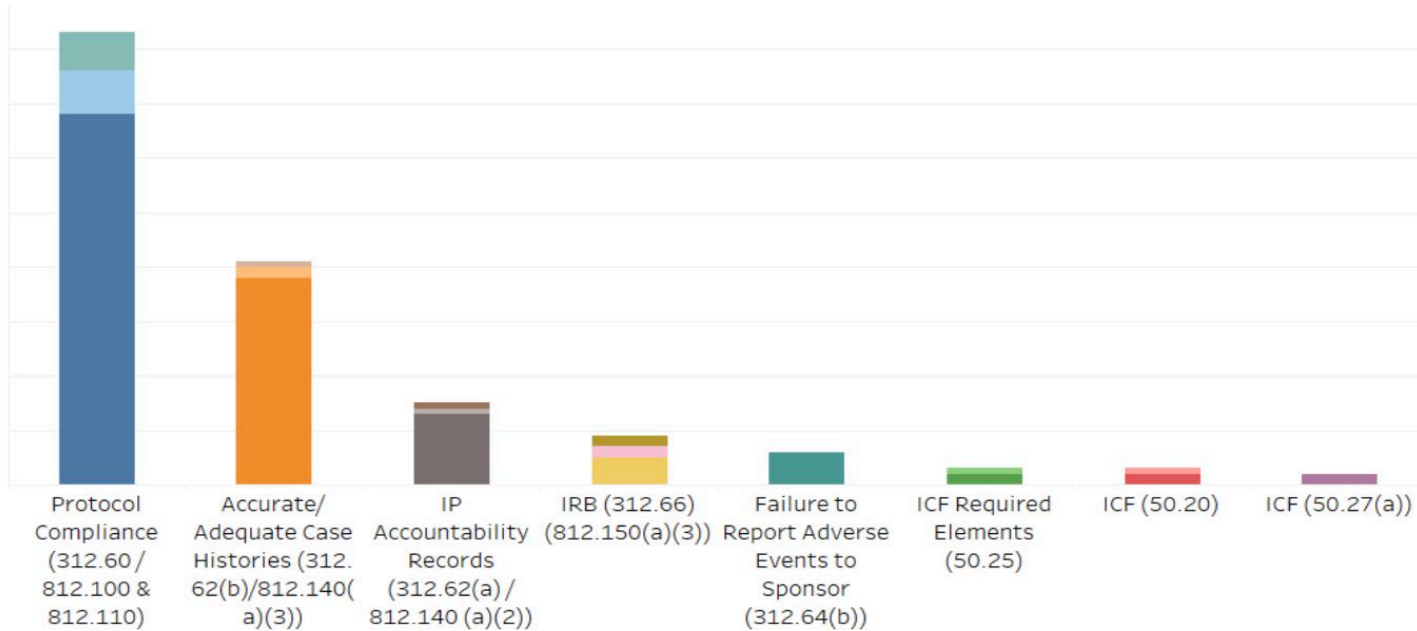


Why is this important?

COMMON Clinical Investigator Inspectional Observations collected from issued FDA Form 483s FY2022:

- Failure to comply with Form FDA 1572 requirements, protocol compliance
- Failure to follow the investigational plan; protocol deviations
- Inadequate and/or inaccurate case history records; inadequate study records
- Inadequate accountability and/or control of the investigational product
- Safety reporting; failure to report and/or record adverse events
- Inadequate subject protection; informed consent issues

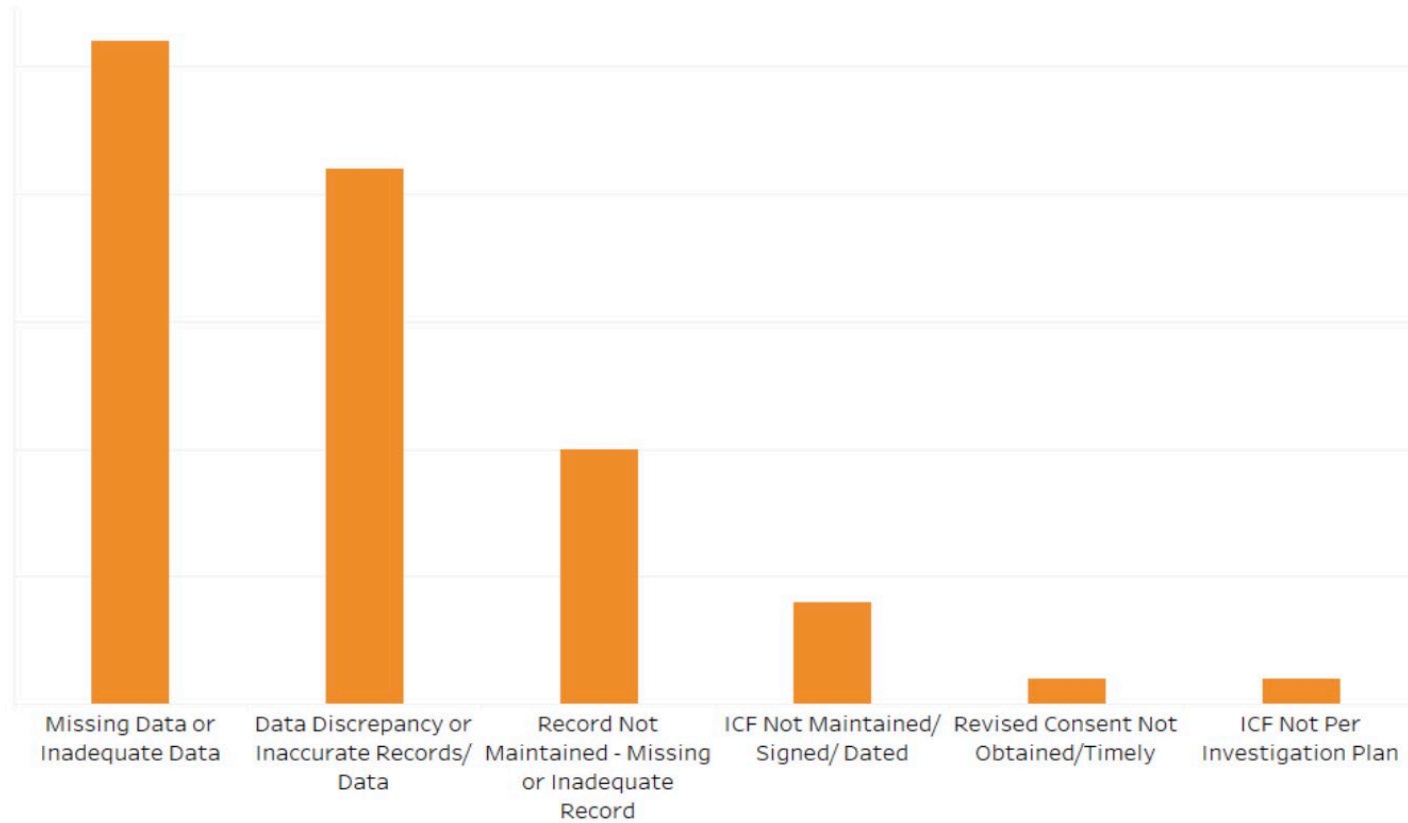
FY 2022 Most Common Clinical Investigators 483 Short Cites by Theme



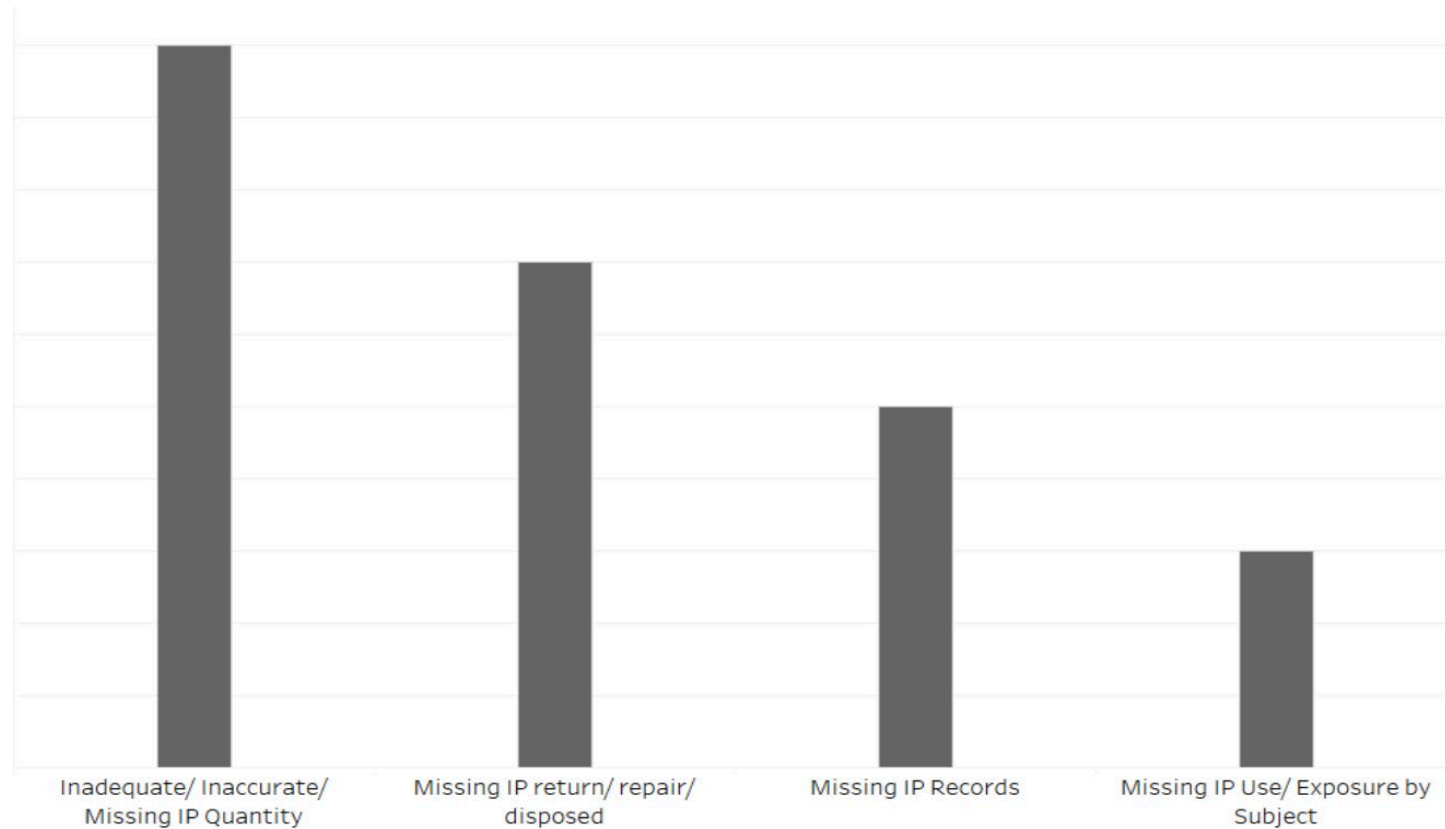
Short Cite Description

- Informed consent
- Non-compliance w/ agreement/plan/regulations
- FD-1572, protocol compliance
- Investigator adverse effect records inadequate
- Investigator's subject records inadequate
- Case history records- inadequate or inadequate
- Investigator device accountability inadequate
- Records of disposition of devices inadequate
- Accountability records
- Initial and continuing review
- Changes in research
- Unanticipated problems
- Safety reports
- ClincialTrials.gov statement
- No statement of experimental procedures
- Understandable language
- Circumstances of obtaining consent
- Consent form not approved/signed/dated

Accurate/Adequate Case Histories (312.62(b)/812.140 (a)(3)) Theme Details



IP Accountability Records (312.62(a) / 812.140(a)(2)) Theme Details



Our experience with common audit findings

- Not following ALCOA-C
- Missing or incomplete source documents
- Discrepancies between source data and case report form
- Missing or inadequate ICF process and eligibility documentation
- Inadequate drug accountability documentation

“IF IT WASN’T DOCUMENTED, IT WASN’T DONE”

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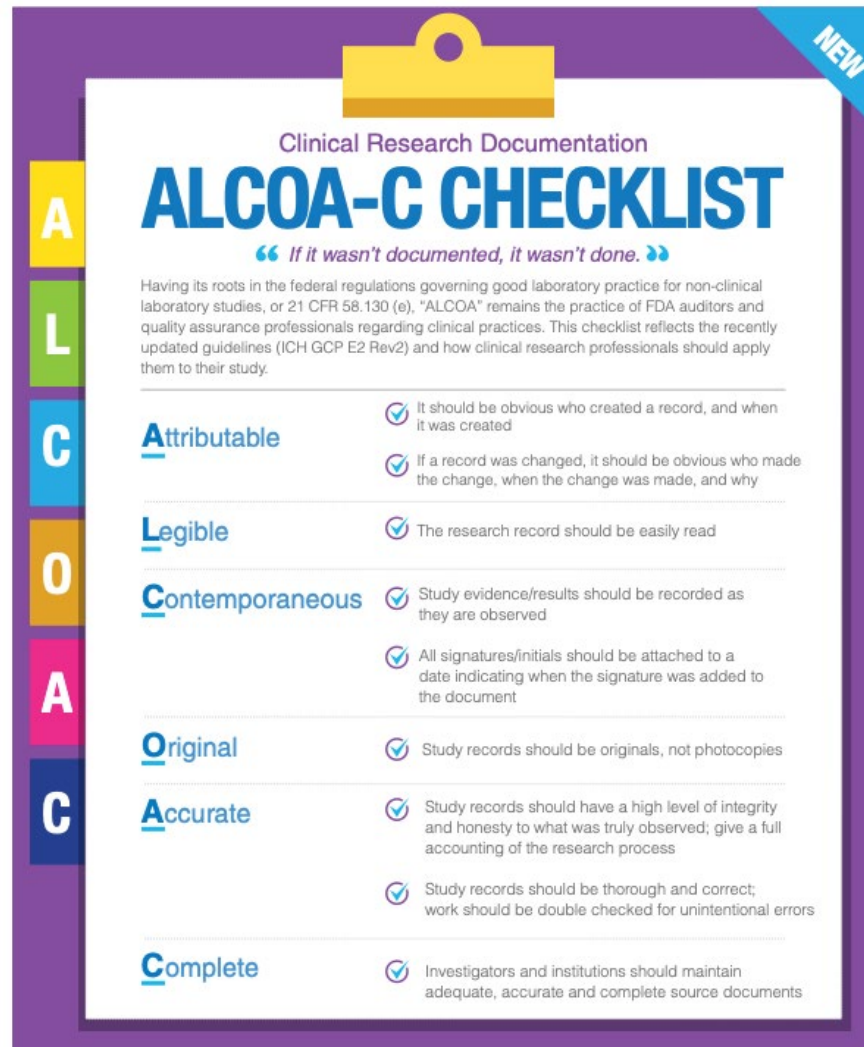
“I understand you gave it all to the poor,
but do you have any receipts?”

GU/MHRI Source Documentation SOP

Check with your institute for your specific SOP or guidance

- GU/MHRI Joint Procedure MG.O-004.10 — Source Documentation (Version 5/11/20)
- Purpose – Provide research personnel guidance regarding source documentation
- Scope – Applies to all designated individuals and research staff responsible for documenting source data in human subject research

How do you ensure good source documentation practice?



The graphic is a checklist titled "Clinical Research Documentation ALCOA-C CHECKLIST". It features a purple border with a yellow clip at the top and a blue "NEW" banner in the top right corner. On the left side, the letters A, L, C, O, A, C are arranged vertically in colored boxes. The checklist items are: **A** Attributable, **L** Legible, **C** Contemporaneous, **O** Original, **A** Accurate, and **C** Complete. Each item has a corresponding checkmark and a brief description of the requirement.

Clinical Research Documentation

ALCOA-C CHECKLIST

“ If it wasn’t documented, it wasn’t done. ”

Having its roots in the federal regulations governing good laboratory practice for non-clinical laboratory studies, or 21 CFR 58.130 (e), "ALCOA" remains the practice of FDA auditors and quality assurance professionals regarding clinical practices. This checklist reflects the recently updated guidelines (ICH GCP E2 Rev2) and how clinical research professionals should apply them to their study.

A	Attributable	<input checked="" type="checkbox"/> It should be obvious who created a record, and when it was created
		<input checked="" type="checkbox"/> If a record was changed, it should be obvious who made the change, when the change was made, and why
L	Legible	<input checked="" type="checkbox"/> The research record should be easily read
C	Contemporaneous	<input checked="" type="checkbox"/> Study evidence/results should be recorded as they are observed
O	Original	<input checked="" type="checkbox"/> All signatures/initials should be attached to a date indicating when the signature was added to the document
A	Accurate	<input checked="" type="checkbox"/> Study records should be originals, not photocopies
		<input checked="" type="checkbox"/> Study records should have a high level of integrity and honesty to what was truly observed; give a full accounting of the research process
		<input checked="" type="checkbox"/> Study records should be thorough and correct; work should be double checked for unintentional errors
C	Complete	<input checked="" type="checkbox"/> Investigators and institutions should maintain adequate, accurate and complete source documents

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Applying ALCOA-C

Ask yourself these questions:

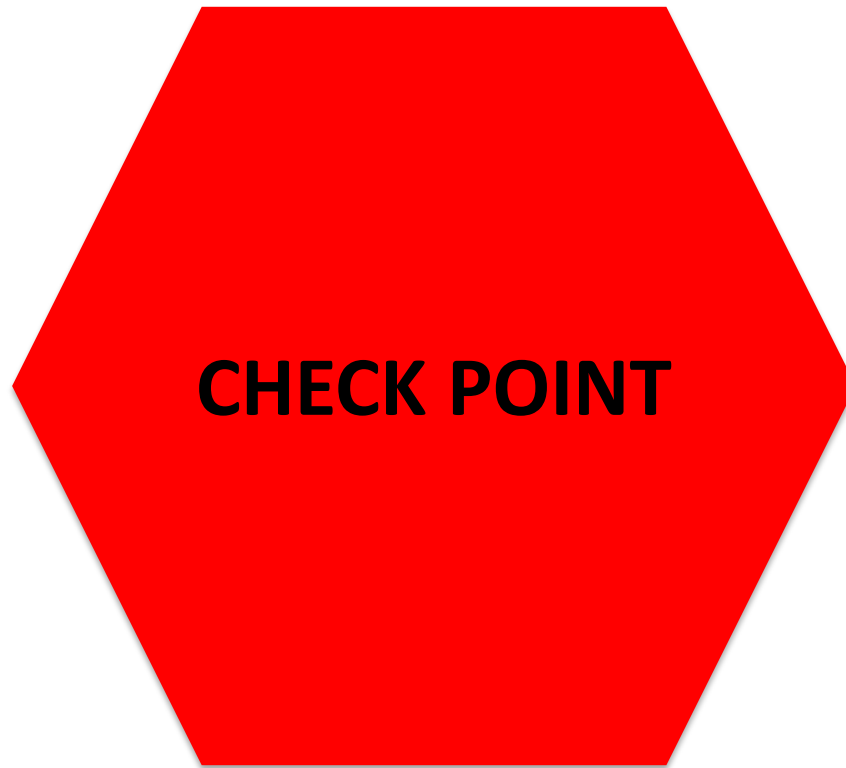
- **Attributable**
 - Who created the information?
 - Who performed the action that gathered the data?
 - When was the record created?
 - Who changed the record? Why was the record changed?
- **Legible**
 - Can it be read?
 - Is it clearly understood?

Applying ALCOA-C

- **Contemporaneous**
 - Is the information current?
 - Was it captured in a timely manner?
- **Original**
 - Is this the original or a photocopy?
 - Has it been altered?
- **Accurate**
 - Is this a correct reflection of study conduct?
 - Is there conflicting data elsewhere?
- **Complete**
 - Is the data and documents adequate and complete?

General Rules

- Do not sign or back date documents
- Do not pre-sign or date blank documents
- Corrections
 - Should not obscure original entry
 - Single line through the incorrect information
 - Dated, Initialed, and explained (if necessary) in real time



CRF Review Activity

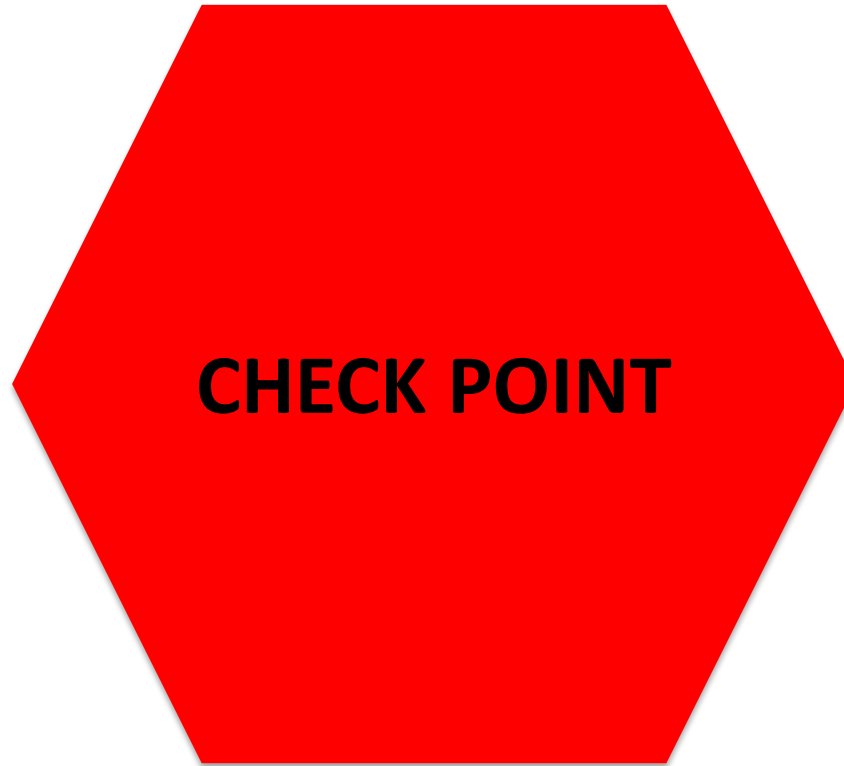
Participant ID: <u>123-001</u>	Date of Visit: <u>01/15/2020</u>	1 Month Study Visit
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Height and Weight		
Time: <u>09:00</u>		
Height: <u>65</u> in	Weight: <u>150</u> kg	
Vitals		
Time: <u>09:03</u>		
Blood Pressure [sitting for 5 minutes] (mmHg): <u>155 / 95</u> NCS		
Pulse (beats/min): <u>75</u>	Respiration (/min): <u>30</u>	Temperature (C): <u>37.</u>
Urine Pregnancy Test <u>NOT COMPLETED</u>		
Time: <u> </u> : <u> </u>		
Completed? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO <input type="checkbox"/> N/A		
Results: <input type="checkbox"/> Positive <input checked="" type="checkbox"/> Negative		
12 Lead Electrocardiogram (EKG)		
Time: <u>09:20</u>		
Was EKG performed? <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO		
Was subject supine for at least 5 minutes? <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO		
EKG Interpretation: <input type="checkbox"/> Normal <input checked="" type="checkbox"/> Abnormal, NCS <input type="checkbox"/> Abnormal, CS		
Lab Collection		
Time: <u>09:30</u>		
Was the scheduled laboratory samples obtained? <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO done by Jane Doe, RN		
AE and ConMed Review		
Time: <u>09:45</u>		
Any changes in medications reported by participant? <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO		
<u>Ibuprofen 200mg every 8 hrs</u>		
Any additional AEs to report since last visit? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO		
(If YES, record AE on Adverse Events page)		

Joe Goldberg Joe Goldberg 01/15/2020

Ensuring Good Documentation Practice

- CRFs
 - Can be used as source documents if they represent the data collected for the study and are where the data is initially recorded
 - Must match data in source documents
 - Protect subject confidentiality
 - Contain clear subject identifiers
 - Must be signed/initialed and dated by the research personnel completing it
 - Always be available for review



TRUE OR FALSE

A COMPLETED CHECKLIST IS SUFFICIENT
SOURCE DOCUMENTATION FOR ELIGIBILITY.

Data Tools

- Checklists
 - Criteria **needs** supporting source documentation
 - Criteria **must** match with the protocol
 - If “no” is checked, documentation of **why**
 - Especially if you created it yourself, QC to match protocol
 - Have a process in place for amendment changes
- Self-Administered Questionnaires
 - Actual data on a completed questionnaire does not need supporting documentation
 - Documentation that the questionnaire was given to the participant
 - Must be maintained as part of the research record

IP Documentation

- Overall IP accountability vs subject accountability
- Can be recorded in the clinic notes
- Best practice: Subject accountability could be recorded on a subject specific accountability log, which could also include compliance % if it serves the protocol
- Could be used as a source

ICF process source documentation

- A fully signed ICF is not enough to document softer elements of the informed consent process.
- Document the ICF process in the EMR or in the subject binder. The statement should include –
 - Discussion
 - Time provided for questions and clarifications were addressed
 - No coercion, voluntary participation
 - No research activities were done prior to obtaining consent
 - Copy provided to participant
- MedConnect has an autotext function to include this narrative

ICF sample narrative note

Attachment B

Sample Narrative Note for Documenting Informed Consent Process

if not using MedConnect AutoText

Name: John Smith
Short Title: DP1822 CHAC

The above-named patient has volunteered to participate in the above-named research study. This patient was counseled about their part in the participation of the research study and I have reviewed and discussed the informed consent form provided. This patient was given reasonable time to consider their decision to become a research subject in the absence of coercion or undue influence. The patient was given an opportunity to have their questions about the clinical trial and/or involved medical procedures answered. An investigator was available during the informed consent process to discuss the trial's risks, benefits and other aspects with the potential subject.

In accordance with HIPAA, a Medical Records Release and General Authorization to Use and Disclose Health Information for Research was reviewed with, granted and signed by the patient.

In accordance with FDA informed consent Regulations (21 CFR 50.27), the patient has been provided with a signed copy of the Informed Consent Form, which they have signed, after reading it or having it read to them. A copy will also be filed in the patient's medical record.

No study related procedures were performed prior to the subject signing informed consent. Contact information was given to the patient.

Name and Signature of Person Obtaining Consent: Mary Jones
Date of Informed Consent: August 18, 2019
Informed Consent IRB Approval Date: July 22, 2019
Time of Consent: 1:30 pm

Use of e-signatures on source documents

- FDA-regulated trials should use 21 CFR part 11 compliant signatures
- Ensure you are using your institute's compliant signature platform
- Do not use scanned signatures on source documents

Certified Copies

- A scanned copy of a source document is not a 'certified copy'.
- A certified copy is defined as a copy of original information that has been verified as an exact copy having all of the same attributes and information as the original. A certified copy (irrespective of the type of media used) of the original record 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.
- Ensure there is an institutional/departmental SOPs in place for creation and storage of certified copies.

Certified Copies

- Once you have an approved SOP in place for this purpose, you would be able to destroy the original
- Otherwise, you should not destroy original documents even if you made copies
- For FDA regulated research, your electronic storage platform should also be 21 CFR Part 11 compliant

Electronic Case Report Form (eCRF) in Clinical Investigations

Electronic case report form acts as the 'trial machine' used to assemble all trial data.

- Data can enter the eCRF from many different sources: investigators, study staff, clinical labs, patient reports, imaging facilities, bar code readers, electronic health record systems and devices etc.
- Each data element entering the system needs to be tagged
 - a data originator (the person or machine entering the data)
 - the date and time
 - a patient identifier

Difference between original and transcribed data



- If a data originator measures a blood pressure, or reports abdominal pain or the presence of a rash, the electronic data entry into the electronic case report form suffices the need.
- If a data originator transcribes a finding from a radiology report or a lab report, the original record must be kept.

Use of EHR in research

- Source documents can be generated and stored in the EHR – examples include ICF process notes, clinic notes, adverse event documentation
- “FDA does not intend to assess compliance of an electronic health record (EHR) system with part 11 regulations because, in general, they are under the control of organizations not regulated by FDA (e.g., health care providers, health care organizations, and health care institutions).” – FDA Guidance Electronic Systems, Electronic Records, and Electronic Signatures in Clinical Investigations Questions and Answers

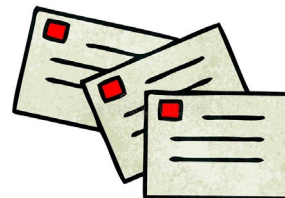
Potential Advantages of the Use of EHRs in Clinical Investigations

- Improve data accuracy
- Promote clinical trial efficiency
- Access to many types of data that can be combined, aggregated, and analyzed
- Access to real-time data for review
- Facilitate post-trial follow-up
- For long-term follow up of large numbers of patients



Relevant Communication

- Letters, emails, and progress notes must be maintained in the participant chart
- Notes of telephone calls and all contact attempts should be documented



Note to File (NTF)

- Identify a discrepancy or problem in the conduct of the clinical research study.
 - Must include: the root cause, the corrective action, and that the corrective action has resolved the problem
- Document the reason for missing, delayed or erroneous documents in the regulatory binder.
- Explain protocol deviations or investigator site practices that are different from the protocol.

Note to File



“Generation of memos to file does not adequately secure compliance of an investigator”

How can we ensure good source documentation?

PRIOR TO START OF STUDY

DURING THE STUDY

AT STUDY COMPLETION



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Who holds responsibility?

- PI holds **main** responsibility and is held accountable
 - PI may delegate tasks with the completion of source documentation to qualified research members, but may not delegate the responsibility or accountability

Summary

- Source documents consists of original documents, records and data that helps to reconstruct the trial as it happened and confirm the data
- Ensures protection of subjects and confirms data integrity and compliance
- Source documentation should demonstrate the ALCOA-C and other attributes as described by regulatory authorities and GCP
- Electronic signatures and electronic storage– For FDA regulated research use 21 CFR Part 11 compliant platforms

Scenario 1

Name: Mrs. Jane Smith

Short Title: DP1822 CHAC

The above named patient has volunteered to participate in the above named research study. This patient was counseled about their part in the participation of the research study and I have reviewed and discussed the informed consent form provided. This patient was given reasonable time to consider their decision to become a research subject in the absence of coercion or undue influence. English was not this patient's primary language.

The patient was given an opportunity to have their questions about the clinical trial and/or involved medical procedures answered. An investigator was available during the informed consent process to discuss the trial's risks, benefits and other aspects with the potential subject.

In accordance with FDA informed consent Regulations (21 CFR 50.27), the patient has been provided with a copy of the Informed Consent Form. A copy will also be filed in the patient's medical record.

No study related procedures were performed prior to the subject signing informed consent. Contact information was given to the patient.

Ideal scenario considerations

- If an interpreter or translator was utilized
- Witness
- Translated ICF or short forms
- Who signed what

Scenario 2

- At the first visit you dispensed a bottle with 60 pills to be taken twice a day starting next day. You instruct the participant to bring back the bottle at the next visit. How will you document this?
- The participant comes in 30 days later for Visit 2. You count the return and there are 40 pills remaining. How will you document this?

Considerations

- Use a subject-specific drug accountability log to maintain dispensation and compliance records in an ongoing fashion
- % compliance is less than 50% - re-education/counselling regarding compliance
- Ask participants if they have trouble with the regimen or drug administration (if this example had injections/pumps/sprays)

Study Information: Protocol or IRB Number, PI Name, Protocol title
DRUG DISPENSATION & ACCOUNTABILITY LOG

Subject Initials:

Subject ID:

Visit #	Number of Units Dispensed (ex. No. of tabs/vials/ml etc.)	Dose Dispensed	Date Dispensed	Dispensed by (staff initials)	Expected Date of First Dose	Number of Units Returned	Date Returned	Verified by (Staff initials)	Actual number of units used/taken	Estimated number of units to be used/taken	% Compliance
1	1 Bottle/30 tablets	20mg	06/01/23	DM	06/01/23	5 tablets	06/30/23	DM	25	30	83%

At end of study: PI Signature: _____ Date: _____



Scenario 3

- Patient meets with the CRC for research labs and complains of nausea and weakness. They are scheduled to meet with the PI later in the day. What would the next steps be here?

Considerations

- Ensure the PI is aware of this information.
Sometimes participants don't repeat the same info.
- Adverse event assessment by the PI
- Documenting the AE in an adverse event log. If determined to be an SAE, follow reporting guidelines
- Updating concomitant medication log if participant self-medicated or if PI prescribed any medications

References

- ICH-GCP E6 (R2)
- Guidance for Industry: Electronic Source Data in Clinical Investigations -
<https://www.fda.gov/media/85183/download>
- Guidance for Industry: Use of Electronic Health Record Data in Clinical Investigations -
<https://www.fda.gov/media/97567/download>
- MG O-004.10 Source Documentation SOP
- ALCOA-C guidelines
- 21 CFR Part 11 – Electronic records; Electronic signatures

Questions?

