BU Clinical & Translational Science Institute

Research Professionals Network Workshop Series

BEST PRACTICES IN STUDY DOCUMENTATION

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- What is the *product* of your study?
- *Data* supports the study hypothesis.
- What *supports* your study data?

Are Poor Documentation Practices in Clinical Research a Problem?

Yes they are……

- **"The failure to keep adequate/accurate records is one of the 5 most common observations that FDA inspectors find at clinical sites…"**

Quote from industry expert in Guide to Good Clinical Practice, Feb 2008

- **'Inadequate records' was the 2nd to highest investigator deficiency in FY 2015 CDER Inspections**

Good Clinical Practice Q&A Reference Guide, May 2016

Study Documentation

Patient Care:
If it wasn't documented, it wasn't done.

Research:
If it wasn't documented, it wasn't done….. AND the data cannot be validated.

Workshop Objectives

- Review the *purpose* of documentation in clinical research
- Differentiate between different *types* of documentation used in clinical research
- Apply *best practices* in study documentation

Purpose of Study Documentation

Common Rule 45 CFR 46	**Documentation of participant consent (unless waived by IRB), and that copy of ICF given to subjects**
21 CFR 312.62(b)	**An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered drug or employed as a control in the investigation….”**
ICH GCP	**“…those documents that individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced.”** -Serve to demonstrate compliance of the investigator, sponsor, and monitor with the standards of GCP and all applicable regulatory requirements.” (ICH GCP 8.1) -ICH GCP (E6) part 8 - Essential Documents for Conduct of a Clinical Trial

Purpose of Study Documentation

BMC/BU Med Campus HRPP P&P	Obtaining and documenting informed consent; Adhering to and document adherence to approved inclusion and exclusion criteria; Maintain all required records; Documenting response to subjects

Documentation Vocabulary

Source Data	Data that includes clinical findings, subject observations and evaluations (ex. Diagnosis, BP, height/weight, subject interviews, lab results, etc). **Source Data must be attributable to the person who obtained/collected
Source Documents (Data Collection Forms)	The original record (and certified copies) that contains the source data (EMR, data collection form, sticky note, lab report, etc.)
Case Report Forms (CRF)	Protocol specific document created as a data collection/transmission tool (can be paper or electronic) Provides a way to record study data in a clear logical consistent manner so data from different participants and from different sites can be analyzed.
Checklists	Tool that can be used to document/verify that study procedures were completed (including documentation to support they were done)
ALCOA	Documentation Standard utilized in ICH GCP as well as FDA CGMP.

Source documentation should:

- Source documentation in a clinical trial should reconstruct the trial as it happened.
- Tell the story of the subject's participation in the study and the conduct of the study.
- Allow you to know **who** did **what** study activity **when**…and **what** data was generated.
- Allow for an individual with basic knowledge of the study to recreate the events of the study.

CRFs and Source Documents

- Data on source documents must match data listed on the CRFs.
- Data on CRFs must have source document to verify the data…. *unless:*
  - If source data is entered directly onto CRFs, this should be prospectively identified in the trial design/protocol *(ICH GCP 6.4.9).*
  - **If CRF serves also as source document, the data must be attributable**… signature or initials and date is necessary from the person who collected that data.

Checklists

- A tool to help ensure that all procedures/assessments for a study visit have been completed.
- Placed in participant binder at front of visit tab with supporting source documents following.
- Where else in clinical trials do we routinely see a checklist used in a clinical trial?

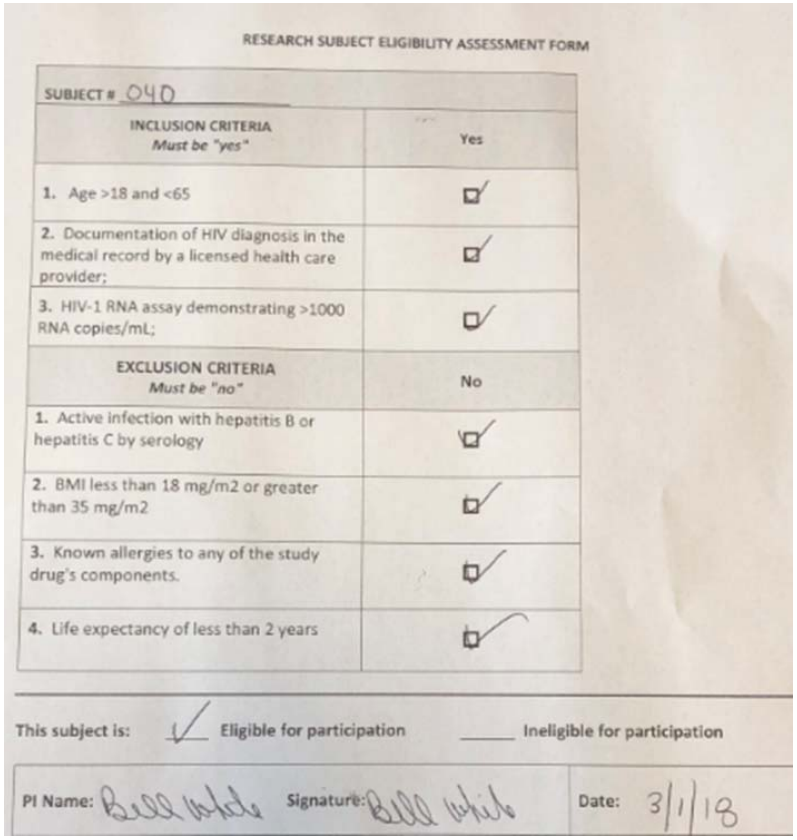
ABC Study Visit 1 Checklist	
Participant #:_____ Date of Visit:_____	
Procedure/Assessment	**Completed**
Inclusion/Exclusion Assessment	☐
Blood Labs collected and sent to lab	☐
Participant Randomized	☐
Participant Provided Study Drug and Diary	☐
Participant Reimbursement Payment/Clin Card	☐
Study Visit Data Updated eCRF	☐

Checklist for Assessment of Participant Eligibility

- Checking off the box to indicate that participant meets eligibility criteria is not sufficient source documentation to validate that participant met each criterion.

- There must be source documentation available for each inclusion/exclusion. That source documentation must be attributable to the person who collected information and/or made determination.

Eligibility Criteria – Source Documentation



RESEARCH SUBJECT ELIGIBILITY ASSESSMENT FORM

SUBJECT # 040

INCLUSION CRITERIA *Must be "yes"*	Yes
1. Age >18 and <65	☑
2. Documentation of HIV diagnosis in the medical record by a licensed health care provider;	☑
3. HIV-1 RNA assay demonstrating >1000 RNA copies/mL;	☑
EXCLUSION CRITERIA *Must be "no"*	**No**
1. Active infection with hepatitis B or hepatitis C by serology	☑
2. BMI less than 18 mg/m2 or greater than 35 mg/m2	☑
3. Known allergies to any of the study drug's components.	☑
4. Life expectancy of less than 2 years	☑

This subject is: ✓ Eligible for participation ____ Ineligible for participation

PI Name: Bill White Signature: Bill White Date: 3/1/18

What source data/documentation is needed to validate each eligibility criterion?

-Age >18 and <65
-Documentation of HIV diagnosis in the medical record by a licensed health care provider;
-HIV-1 RNA assay demonstrating >1000 RNA copies/mL;

-Active infection with hepatitis B or hepatitis C by serology
-BMI less than 18 mg/m2 or greater than 35 mg/m2
-Known allergies to any of the study drug's components.
-Life expectancy of less than 2 years

Source Documentation
Group Activity

Documentation of Pregnancy Testing

-or-

Determination that Pregnancy Testing Is Not Required

Participant ID #:	_____
Participant Age:	_____
Study Visit:	_____

Pregnancy Test Completed:	☐ Yes ☐ No
If Yes, complete the following:	Date of test:_____ Time:_____
Type of Test	☐ Urine ☐ Blood
Test Result	☐ Negative ☐ Positive
Tests Results Located:	☐ Attached ☐ EMR ☐ Other, Specify_____
If No Pregnancy Test, Reason	☐ Hysterectomy Date of hysterectomy:_____ ☐ Post-Menopausal Date last menstrual period: _____ Post-Menopausal(non-surgical) is at least 12 months after a woman's last period.
	☐ Other Reason, specify: _____
Notes/Comments:	

Study Staff Name: _____

Signature: _____ Date: _____
(signature is required even if pregnancy test not done)

Documentation Best Practices

Best Practices

Prior to start of study:

-*Determine* what source data will be needed and where it will come from (EMR, subjects: PE, vitals, interview/self-report).

-*Develop* source data collection forms if not provided by sponsor.

- *Review and compare* source data collection forms them with the Sponsor Protocol.

-Make sure study staff collecting source data are *qualified, trained and delegated* by PI.

Best Practices in Study Documentation

During Study:

-Each time there is a protocol change, *compare* CRFs and source data collection forms and checklists with changes and modify forms as needed.

-Make sure that all staff are *aware* of changes to protocol and new/revised CRFs or data collection forms.

-If applicable, have PI *re-assess* staff delegation.

Optional (highly recommended!):

-*Conduct* a targeted Study Self-Assessment early on during enrollment with focus on documentation.

Best Practices in Study Documentation

Study Completed:

-Communicate study completion to participants and send any correspondence.

-Document any correspondence with subjects.

-Know Sponsor and institutional requirements for storage of documentation.

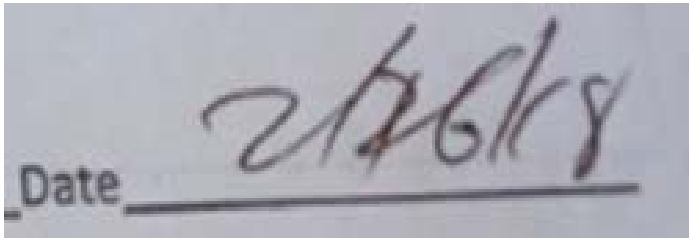
ALCOA Documentation

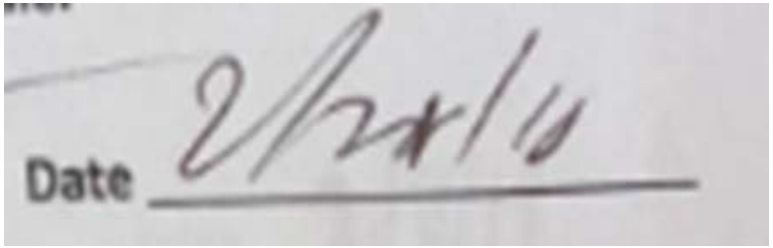
Source Documentation should always adhere to ALCOA Documentation Standards

ALCOA Documentation Standards

Attributable	Be clear who has documented the data
Legible	Capable of being read Changes don't obscure original entry Signatures should be legible
Contemporaneous	The documentation, signature, and date need to be completed at the same time and as close to the event as possible
Original	First recording of the information (paper, electronic)
Accurate	Consistent, real representation of facts Errors have been identified and corrected with notes to explain if needed

Legible?





Original?

Study RA forgot to bring Vital Sign Source Data Collection Form to GCRU for study participant #001 study visit on 5/1/18. RA noted vitals on a sticky note. Once back at the office the RA transferred the vital data to the collection form. **Can the RA throw away the sticky note?**

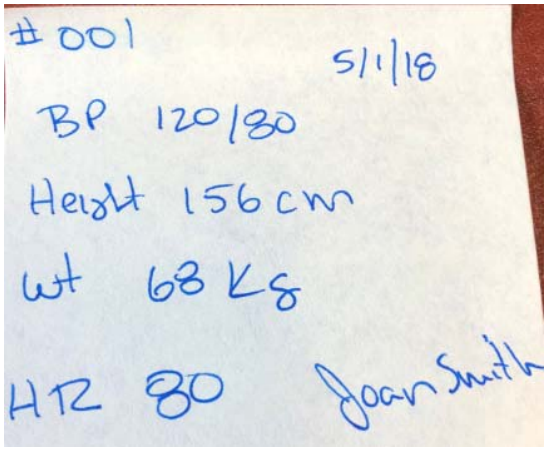
ABC Study
Visit 1 Source Data Collection Form/CRF

Participant ID#: 001

Vitals/Urine Pregnancy Testing

BP: 120/80 Height: 156 cm Weight: 68 Kgs Heart Rate: 80

Urine Pregnancy Test Completed: __YES ___NO X N/A Results: __Positive __Negative

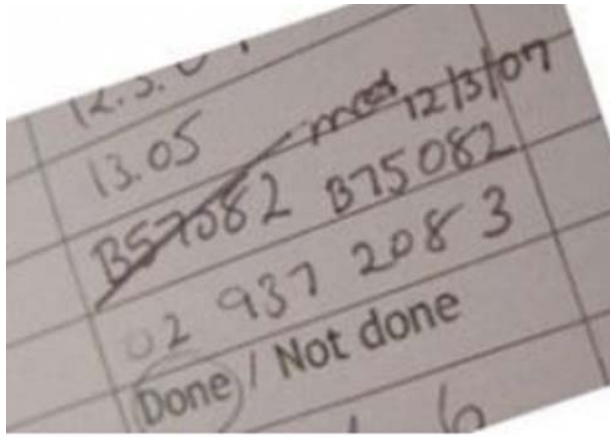


Corrections to Study Documentation

Corrections are expected!

Proper Corrections:

- One line through error, write new data, initial, date and explain (if necessary)
- Entries on study documents and changes to those entries should be made by study team members with the *authority* to do so as delegated by the PI.

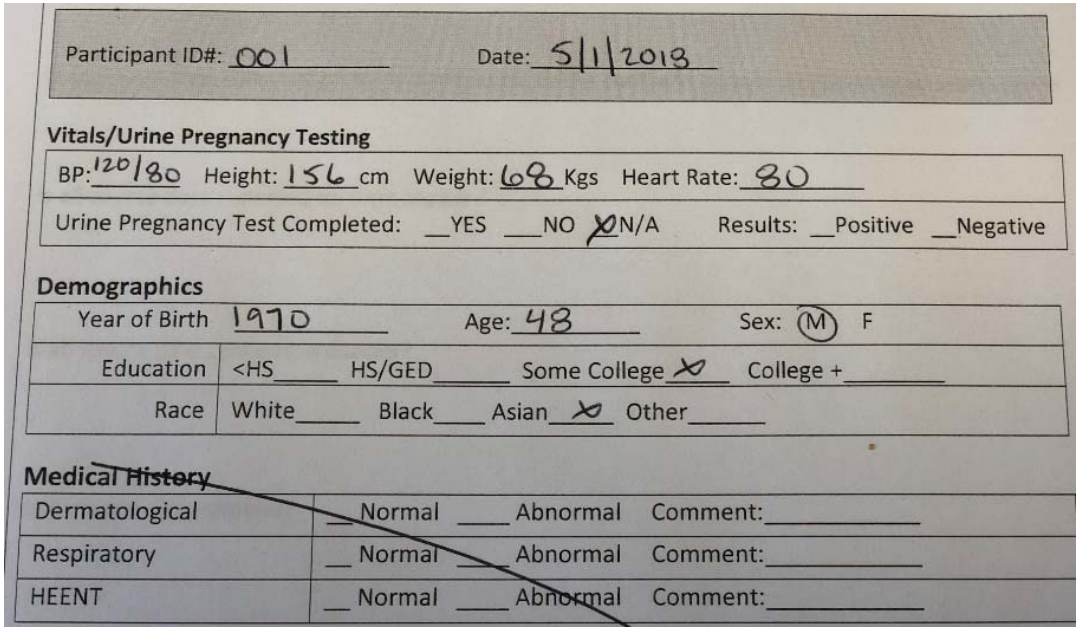


Unacceptable Corrections:

- Complete cross-out, correction fluid, write overs
- New information must not obliterate previous information
- Erasing/Recording in pencil
- Editing subject's personal writings or responses on forms

Additional Best Practices

- Document ***what is*** and ***what is not*** done, include reasons for any missed information.



Participant ID#: 001 Date: 5/1/2013

Vitals/Urine Pregnancy Testing

BP: 120/80 Height: 156 cm Weight: 68 Kgs Heart Rate: 80

Urine Pregnancy Test Completed: __YES ___NO X N/A Results: __Positive __Negative

Demographics

Year of Birth 1970 Age: 48 Sex: (M) F

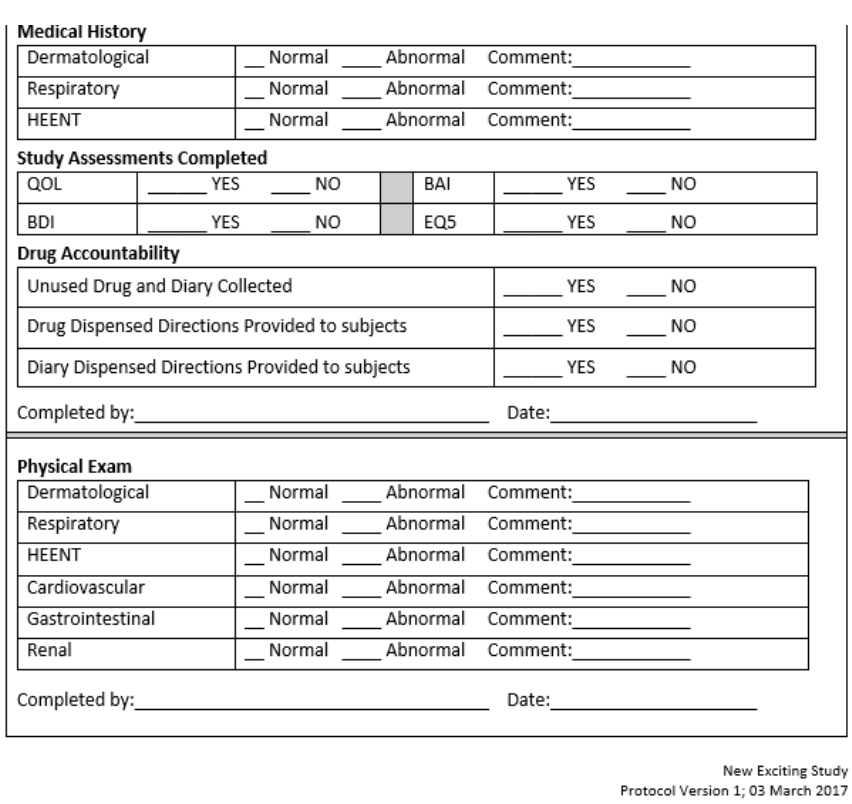
Education <HS____ HS/GED_____ Some College X College +_____

Race White____ Black____ Asian X Other_____

Medical History

Dermatological	__Normal ____Abnormal	Comment:_____
Respiratory	__Normal ____Abnormal	Comment:_____
HEENT	__Normal ____Abnormal	Comment:_____

Additional Best Practices



Medical History

Dermatological	__ Normal ____ Abnormal	Comment:_____
Respiratory	__ Normal ____ Abnormal	Comment:_____
HEENT	__ Normal ____ Abnormal	Comment:_____

Study Assessments Completed

QOL	_____ YES ____ NO		BAI	_____ YES ____ NO
BDI	_____ YES ____ NO		EQ5	_____ YES ____ NO

Drug Accountability

Unused Drug and Diary Collected	_____ YES ____ NO
Drug Dispensed Directions Provided to subjects	_____ YES ____ NO
Diary Dispensed Directions Provided to subjects	_____ YES ____ NO

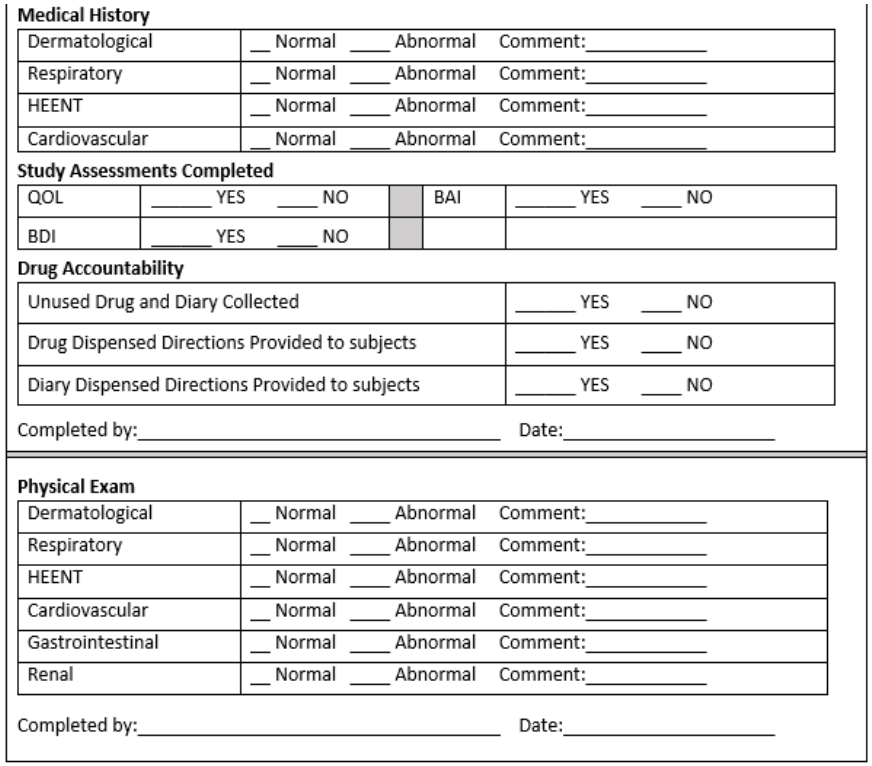
Completed by:_____ Date:_____

Physical Exam

Dermatological	__ Normal ____ Abnormal	Comment:_____
Respiratory	__ Normal ____ Abnormal	Comment:_____
HEENT	__ Normal ____ Abnormal	Comment:_____
Cardiovascular	__ Normal ____ Abnormal	Comment:_____
Gastrointestinal	__ Normal ____ Abnormal	Comment:_____
Renal	__ Normal ____ Abnormal	Comment:_____

Completed by:_____ Date:_____

New Exciting Study
Protocol Version 1; 03 March 2017



Medical History

Dermatological	__ Normal ____ Abnormal	Comment:_____
Respiratory	__ Normal ____ Abnormal	Comment:_____
HEENT	__ Normal ____ Abnormal	Comment:_____
Cardiovascular	__ Normal ____ Abnormal	Comment:_____

Study Assessments Completed

QOL	_____ YES ____ NO		BAI	_____ YES ____ NO
BDI	_____ YES ____ NO			

Drug Accountability

Unused Drug and Diary Collected	_____ YES ____ NO
Drug Dispensed Directions Provided to subjects	_____ YES ____ NO
Diary Dispensed Directions Provided to subjects	_____ YES ____ NO

Completed by:_____ Date:_____

Physical Exam

Dermatological	__ Normal ____ Abnormal	Comment:_____
Respiratory	__ Normal ____ Abnormal	Comment:_____
HEENT	__ Normal ____ Abnormal	Comment:_____
Cardiovascular	__ Normal ____ Abnormal	Comment:_____
Gastrointestinal	__ Normal ____ Abnormal	Comment:_____
Renal	__ Normal ____ Abnormal	Comment:_____

Completed by:_____ Date:_____

New Exciting Study
Protocol Version 3; 03 May 2018

- Use footers with version numbers and dates whenever possible

Additional Best Practices

- Never *back* or *future* date documents – use current date when entries are made (explain date discrepancies as needed)

- Study teams often make their own source data collection forms from ones used for other studies - Review the new source data collection forms carefully to ensure match sponsor protocol.

Questions/Comments?

ALCOA Activity

Documentation Templates Available on the CRRO Website

- Research Subject Eligibility Assessment Form
- Documentation of Informed Consent Tool
- Documentation of Pregnancy Testing
- Regulatory Binder Documentation Tools (Training, Delegation, AE Tracking, etc)
- Study Self-Assessment Review Tools

http://www.bumc.bu.edu/crro/

Boston University Medical Campus and **Boston Medical Center**:
Clinical Research Resources Office