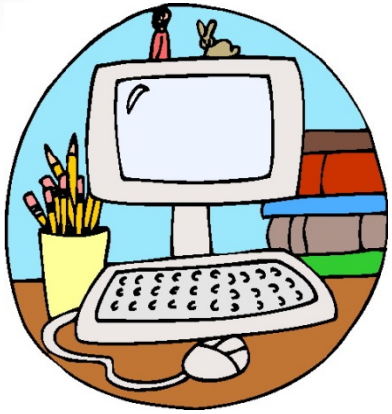


Research Documentation Requirements & Best Practices

IRB Education Meeting

March 17, 2015

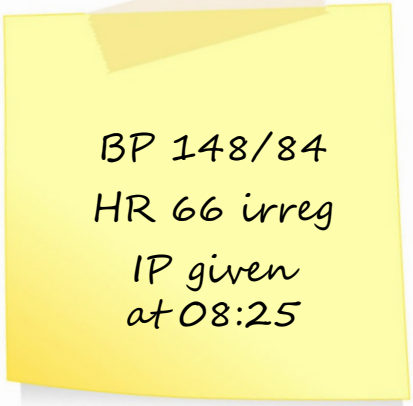
What's the Point?

- Good documentation is needed to provide adequate protection of the rights, welfare, and safety of human subjects and to ensure the quality and integrity of the research data.

- Documentation and records-related issues are the second-most commonly cited deficiency in FDA GCP compliance investigations of clinical trial investigators and sites (after failure to adhere to the clinical protocol).

Source Data/Documents

- ***Source Data*:** All information in original records of clinical findings, observations, or other research activities that are used in a research project. Source data are contained in source documents.
- ***Source Documents*:** Where data regarding study subjects are **first recorded** and serve as the basis for the information that is used in a research project.
  - Common source documents are participant medical records, phone encounters or notes, lab and diagnostic test results, participant diaries, and specific research worksheets used to document key research data elements. **Even sticky notes, paper towels, napkins, etc., must be kept if that's where data was first recorded.**
  - If data are entered directly into a computer, the electronic record is considered the source.

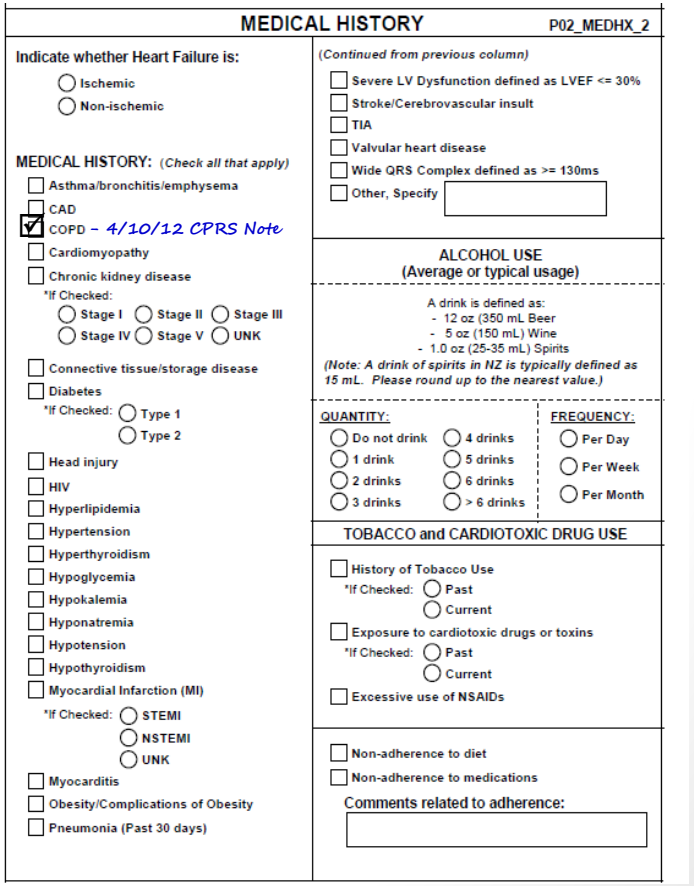


Source Documentation

Each data point necessary to reconstruct and evaluate the conduct of a study must be supported by and traceable to a previously recorded entry in a primary source document.

- All documents should include the date, the event, and the person to whom they are related.
- Every substantive contact with study subjects (e.g., all study visits, phone contacts that require action or contain clinically significant information, etc.) should be documented in the medical record or the study file.

Add a header. Document the primary source of data on the worksheet.



MEDICAL HISTORY P02_MEDHX_2

Indicate whether Heart Failure is:
- ◯ Ischemic
- ◯ Non-ischemic

MEDICAL HISTORY: *(Check all that apply)*
- ☐ Asthma/bronchitis/emphysema
- ☐ CAD
- ☑ COPD – 4/10/12 CPRS Note
- ☐ Cardiomyopathy
- ☐ Chronic kidney disease
  - *If Checked: ◯ Stage I ◯ Stage II ◯ Stage III ◯ Stage IV ◯ Stage V ◯ UNK
- ☐ Connective tissue/storage disease
- ☐ Diabetes
  - *If Checked: ◯ Type 1 ◯ Type 2
- ☐ Head injury
- ☐ HIV
- ☐ Hyperlipidemia
- ☐ Hypertension
- ☐ Hyperthyroidism
- ☐ Hypoglycemia
- ☐ Hypokalemia
- ☐ Hyponatremia
- ☐ Hypotension
- ☐ Hypothyroidism
- ☐ Myocardial Infarction (MI)
  - *If Checked: ◯ STEMI ◯ NSTEMI ◯ UNK
- ☐ Myocarditis
- ☐ Obesity/Complications of Obesity
- ☐ Pneumonia (Past 30 days)

(Continued from previous column)
- ☐ Severe LV Dysfunction defined as LVEF <= 30%
- ☐ Stroke/Cerebrovascular insult
- ☐ TIA
- ☐ Valvular heart disease
- ☐ Wide QRS Complex defined as >= 130ms
- ☐ Other, Specify

ALCOHOL USE
(Average or typical usage)

A drink is defined as:
- 12 oz (350 mL Beer
- 5 oz (150 mL) Wine
- 1.0 oz (25-35 mL) Spirits

(Note: A drink of spirits in NZ is typically defined as 15 mL. Please round up to the nearest value.)

QUANTITY:
- ◯ Do not drink
- ◯ 1 drink
- ◯ 2 drinks
- ◯ 3 drinks
- ◯ 4 drinks
- ◯ 5 drinks
- ◯ 6 drinks
- ◯ > 6 drinks

FREQUENCY:
- ◯ Per Day
- ◯ Per Week
- ◯ Per Month

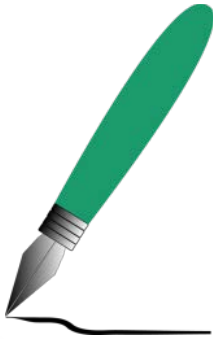
TOBACCO and CARDIOTOXIC DRUG USE
- ☐ History of Tobacco Use
  - *If Checked: ◯ Past ◯ Current
- ☐ Exposure to cardiotoxic drugs or toxins
  - *If Checked: ◯ Past ◯ Current
- ☐ Excessive use of NSAIDs

- ☐ Non-adherence to diet
- ☐ Non-adherence to medications

Comments related to adherence:

Source Documentation

- Source documentation should be timely, i.e., completed as close to the time of observation as possible. Late additions are identified as such.
- Data should not be entered directly onto a case report form (CRF) unless the CRF calls for data not normally recorded on a source document or unless the protocol or operations manual contains instructions to do so.
- If a worksheet is developed to collect study data (or a copy of a CRF is used as a worksheet), it must be labeled **"SOURCE."**



It should always be signed and dated by the person completing the worksheet to document who collected the data.

Source Documentation

- Source documentation should meet the **ALCOA** standard for data quality:
  - **A**ttributable to the person collecting and recording the data
  - **L**egible
  - **C**ontemporaneous (dated and signed/initialed at the same time)
  - **O**riginal (the first recording)
  - **A**ccurate
- When recording the times for a series of study-related activities, **use the same clock** for all events to assure that they were completed in the required order.

General Requirements

Research information is recorded to ensure clarity, traceability, and accountability. Poor documentation can create the perception of non-compliance or fraud.

- Arrows and ditto marks are not acceptable where data is duplicated; each individual line or column must be completed.
- Use permanent ink in entries – never a pencil.
- When a signature and date are required, **the person signing the document must also be the person dating the signature.**
- Never back-date a document.
- Never pre-sign or date a (blank) document (e.g., a consent form that must be mailed to a subject).

General Requirements

- Document what is - and what is not – done, **including reasons for any missed information**.
  - If it isn't documented, it didn't happen.
  - If it didn't happen, don't document it.
- Never fabricate or falsify information, dates, or signatures.
- Beware of copy/paste errors! Templates are good, but **read everything you paste** to make sure it's accurate and nothing is missing (e.g., using previous CPRS notes for a subsequent study visit or for another subject; copying information from a previous research project into an initial IRB application or consent form for a new research project).
- Any form of documentation may be used as a source document and is *subject to review when validating the integrity of data collection and analysis*.

Correcting Errors

- Source documentation must match information on the worksheet. If not, reconcile the discrepancies.
- Corrections are expected but must be entered legibly.
  - Entries on study documents and changes to those entries should only be made by study team members with the authority to do so.
  - Draw a single line through the incorrect information. Don't obscure the original data.
  - Errors must be lined out with a single line; do not use correction fluid/tape, erase or write over data (e.g., turning a 0 into a 9).
  - Enter the correct information, including **your initials and the date corrections were made.**

3/17/2015 M.N. 3/17/2015

Signature: Mysig Nature Date: ~~1/20/1989~~

Documenting Informed Consent

If appropriate for the type of research, include this information with the study records:

- A statement that the subject met qualifying criteria or a completed Inclusion/Exclusion Criteria Checklist (with the subject's name and the PI's signature/date).
- A note in the subject's file or a statement in CPRS that:
  - The consenting documents were reviewed and all questions were answered.
  - **If indicated**, an assessment of the individual's comprehension was conducted *(sample on the next slide).*
  - The subject signed the consent before any study activities were performed.
  - Copies of the signed documents were given to the subject and sent to the IRB for review.

Documenting Comprehension

Search the medical record for clues before contacting the individual.
Assess comprehension by asking open-ended questions, such as:

Purpose

- If your friends and family ask you what the study is about, what would you tell them?

Procedures

- What will be done for the study when you come here? ..when you're at home?
- How long will you be in the study?
- Will you have to make extra trips to the VA?

Risks

- Tell me – or show me in the consent form – the risks of the procedure(s).
- Tell me – or show me in the consent form – the side effects of the study medication.

Research versus Treatment

- Is the research study or medication guaranteed to help you?
- What are the chances that you'll get the active treatment …the placebo?

Contacts

- Show me in the consent form who to call:

  …if you have questions about the study.

  …in case of emergency or if you have distress/discomfort while in the study.

Reasoning:

- What alternative is there if you choose not to participate?

Responses should be documented and filed with the signed consent.

If comprehension is a concern, get a clinical opinion from the PCP or other appropriate clinician before conducting any study procedures.

Recommended ICF Practice

- Some participants are not able to sign their name on consent and HIPAA authorization forms.
- When the subject's signature is indicated on a VA-authorized consent form by an "X," two adult witnesses (preferably not including a study team member) should sign the form.
- Both witnesses should be present when the "X" is placed on the consent form.
- The signatures of these witnesses on the form attests only to the fact that they saw the individual sign the form.

(*VHA Handbook 1004.1 - INFORMED CONSENT FOR CLINICAL TREATMENTS AND PROCEDURES)*

When to Use a Note To File

- A Note To File (NTF) provides additional information or clarification *when other documentation is unavailable or inadequate elsewhere in the research records.*
- A NTF may be used to:
  - Explain the location of a study document when it is not filed in the expected location;
  - Explain a discrepancy, the action taken in response, and the method adopted to prevent similar discrepancies;
  - Clarify an instruction or direction regarding some activity that is required by the protocol but is not clearly explained in the protocol.
- **A NTF is considered source documentation and must be signed and dated** by either the person making the entry and/or the person reviewing and/or validating information.

When NOT To Use a NTF

- Too many Notes To File can raise the concerns of auditors and regulatory inspectors over why there are so many issues with study procedures or study documentation.
- Study personnel should create a NTF *only* if an action, clarification, plan or discrepancy is not addressed fully in other study documents.
- It should never be used as a substitute for prospective and complete source documents.
- NTFs must not be used in place of an *Unanticipated Problem Report* to notify the IRB of a protocol deviation or unanticipated event which presents risk to subject(s) or others.

Other Suggestions

- Documentation should clearly demonstrate that it is the Principal Investigator who is making PI-level decisions – not the study coordinator. The PI should sign and date these records.
- “Official” letters to study subjects should be signed by the Principal Investigator – not the study coordinator.
- Know what is on your Scope of Practice form and revise it if needed. Don’t work beyond the level of authority that has been delegated to you by the Principal Investigator.
- Notify the sponsor when a PI will be away from the site for an extended period and document the interim plan for oversight of research activities during his/her absence.