Documentation and Document Management in Clinical Research

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Objectives

- Describe best practices for clinical research documentation.
- Define and differentiate source documents vs essential documents.
- Discuss how to manage discrepancies among source documents.
- Identify various documents that are considered essential documents.
- Describe when it is appropriate to centralize essential documents and use notes to file.

Why Document

- Communication among the healthcare providers that provides a complete and accurate record of the patient's condition, treatment and response to treatment

One Medical Record, Many Purposes

- A record for reimbursement
- A record for research
- A record for guiding quality improvement
- A record for evidence in legal proceedings
- Regulated by:
  - Federal and state laws
  - Accrediting organizations/JCAHO
  - Licensing statutes
  - Case law
  - Facility policy/procedures

Documentation “Do’s”

- Document all patient encounters
- Use concise, factual, concrete terminology
- Describe reported symptoms accurately
  - Use the patient's words in describing symptoms whenever they might be helpful
- Use acceptable abbreviations
- Describe only what you observed and assessed

Documentation "Don'ts"

- Document in advance
- Chart until the name is checked to confirm correct medical record
- Use slang
- Use medical terms unless their meaning is known
- Chart for anyone else
- Spell words incorrectly

REMEMBER…….

If it was not documented, it was not done or never happened!

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 data are contained in source documents (original records or certified copies).

Source Documents

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 medico-technical departments involved in the clinical trial).

ICH GCP Guidelines E6(R2) Section 1.51 and 1.52

Key Purposes of Source Documents

- Provide original documents, “raw” data and records
- Document existence of the subject
- Substantiate compliance with the protocol and integrity of the study data
- Serve as audit trail = recreate the progression of clinical trial

ALCOA-C

ICH GCP Guidelines E6(R2) Section 4.9
https://go.florencehc.com/l/470131/2019-0327/dhzbxf/470131/98028/Florence_and_ALOCA_C.pdf

Clinical Research Documentation

Documentation acceptable in clinical practice may need additional details when the patient enters a clinical trial.

Research source documentation is never by exception!

General Rules

- All encounters are to be documented in the medical record
  - Ensures good practices
  - Allows for source documents to be available at the time of a data abstraction, monitoring visit or audit
- Conflicting documentation/discrepancies in source documents require a clarification note

Initial Protocol Discussion

- Discussion of protocol(s), associated schemas, adverse events, disease response follow-up, clinic visits, labs, compensation, etc.
- Copy of the appropriate consent form(s) given to participant to review
- Tests done or to be done
- Concerns participant and/or family and how addressed

Informed Consent

- Should be done by all who discussed the study with the subject
- Typically note will include a statement that:
  - A discussion occurred
  - All questions were reviewed and answered to individual's satisfaction
  - A copy of the signed IC document was given to the subject
- HRPP Policy 301: Specific statement in CRIS addressing the informed consent process
- Use structured note in CRIS – *Documentation of Research Consent*

Eligibility Confirmation and Baseline

- All screening results in CRIS and eligibility criteria met including if appropriate:
  - Pregnancy prevention
  - Comorbidities
- All appropriate baseline testing was completed and available in CRIS
- All baseline symptoms including start date and severity
- Review of diary/surveys, how to complete, when to return, etc., if applicable
- All concomitant medications (con meds)

Concomitant Medication

- All con meds that the patient has been taking including:
  - Dates taken – both when started and when stopped or dosage changed
    - Month and Year is acceptable for con meds taken before enrollment
    - Day, month, year is to be noted once enrolled
  - Reason/indication
  - Dosage/Amount in unit of measure
  - Frequency

Scheduled Study Visit…

- Compliance with protocol
- All protocol related visits, procedures, exams, etc. need to be noted in the medical record that they occurred:
  - Document occurrence, results, who conducted and any follow-up (e.g.: PKs drawn, biopsy obtained)
- Missed visits need to be noted including the reason and follow-up

…Scheduled Study Visit

- All adverse events including: date started, date stopped, description of severity, how treated, and attribution to study/drug or study procedures
- All concomitant medications including:
  - Ongoing, Dose changes, New
- Response
- Biospecimen collection

Unscheduled Visit

- All unscheduled study visits, procedures, exams, etc. need to be noted in the medical record including:
  - Reason for visit/procedure
  - Follow-up

Study Drug Administration

- All study drugs administered MUST be recorded in the medical record by the licensed nurse/provider who gave the drug(s)
  - Includes all pre- or post-treatment medications that are listed as study drugs
- Documentation should include:
  - Date, time, amount, route
  - For IV medications, start and stop times
- Missed doses need to be documented including reason

Self-Administered Study Drug

- Subject self-administration of study meds:
  - Instructions for proper use/administration and storage
  - Date and amount dispensed/returned
  - Subject's compliance with regimen

Off-treatment

- Need date subject taken off active treatment and why
- Date is the date when the MD/Investigator decides that no further therapy will be given

Follow-up

- Review and document all protocol-specific activities that occur in the follow-up period.
- May include survival alone or in combination with:
  - adverse events (new and/or unresolved),
  - concomitant meds,
  - tests/procedures conducted,
  - disease/response and/or
  - research labs

Off-study

- Document date and why
- Lost to follow-up:
  - Every attempt should be made to locate patient/subject including:
    - Contact referring physician
    - Contact emergency contact participant identified on admission
    - Send certificated, return receipt letter
    - All attempts should be documented

Telephone Call & E-mail

- Phone Call
  - Document reason for call (adverse event, general question, test result, etc.)
  - Document outcome of call (how adverse event to be treated, etc.)
- E-mail
  - Consent to use FollowMyHealth® patient portal where emails are retained

Documentation Tips

- All licensed individuals need to document all participant encounters in CRIS
- Identifying CRIS structured note:
  - Start a new document. In the left side panel, click on the "Document Info" tab and at the bottom is "Document Topic" box for the entry of a note title or label
  - Consistent labeling of documents, allows for easier sorting, modification, and searching
- QC own notes
- Review other's notes for discrepancies – document clarification of discrepancies
- Educate other team members on quality documentation practices

Document Management: Essential Documents

Essential Documents

- Documents which individually and collectively allow for evaluation of study conduct and the quality of the data produced
- Demonstrate the compliance of the investigator, sponsor and monitor with the GCP and applicable regulations

ICH GCP Guidelines E6(R2) Section 4.9.4

What is a Regulatory File?

- File that organizes the essential documents
- Maintained by both the site and the sponsor
- AKA:
  - Regulatory Files
  - Investigator's Study Files
  - Study Binder
  - Investigator Binder
  - Administrative Binder

Purposes of Essential Documents

- Allows easy access to essential documents by trial monitor, auditor, IRB, or regulatory authorities for review/audit purposes
- Allows research team members to reference information

Maintenance of the Regulatory File

- Principal Investigator is ultimately responsible for maintenance of regulatory files
- This task is often delegated to other members of the research team

Organization of the Regulatory File

- Various formats are acceptable
  - Sponsors may have required format
- Needs to be organized in a manner that allows specific documents to be found easily
- Important rule of thumb with filing is "consistency"

Regulatory File Contents…

- **Protocol and Amendments**
  - Initial protocol and ALL amendments with documented IRB and sponsor approvals
- **Informed Consent**
  - ALL approved versions
- **Continuing Reviews**
  - Approvals from IRB
  - Study completion/termination report

…Regulatory File Contents…

- **FDA Form 1572 for all IND Trials**
  - ALL versions signed and dated
- **Curricula Vitae**
  - Demonstrates qualifications of ALL investigator and sub-investigators, study coordinators
  - Updated copies, may need to be signed and dated

…Regulatory File Contents…

- **Serious Adverse Events**
  - Copies of reports
  - Documentation of receipt from IRB, sponsor, FDA, OBA, as applicable
- **IND Safety Reports**
  - Copies of reports
  - Documentation of receipt from IRB

…Regulatory File Contents…

- **IRB Correspondence**
  - Regarding approval process of protocol, amendments
    - Submissions, stipulations, responses to stipulations
    - Does not need to be entire package
    - Keep enough documentation to provide a trail of the process
  - Regarding continuing review
    - reminder notices
  - Clarifying or stating an issue regarding conduct of the study

…Regulatory File Contents…

- **IRB Membership Lists**
  - IRB composition lists*
- **Subject Identification Code List**
  - Confidential list of the names of all participants with their study Group assigned identification number
  - Maintained only at the site
  - Allows the investigator or institution to quickly identify study participants in the case of an emergency

**IRBO letter stating FWA number , compliance with IRB regulations, and membership lists files as part of NIH's FWA*

…Regulatory File Contents…

- **Investigator's Brochure (IB)***
  - ALL versions of the IB and updates
  - Contains scientific information for investigational product
  - For FDA approved agents, file a copy of the package insert
- **Recruitment advertisements/letters**
  - With documented IRB and sponsor approvals

** All IB versions need to be submitted to the IRB*

...Regulatory File Contents...

- **Sponsor Correspondence**
  - Pre-study correspondence as appropriate
  - Details processes and procedures for study conduct
  - Phone logs
  - Site visit letters/summaries
- **Other Correspondence**
  - Any miscellaneous protocol-related correspondence

...Regulatory File Contents...

- **Laboratory Certification**
  - All copies of CLIA certifications for all labs submitting subject results for purpose of the study
  - Need to have valid certifications filed as long as the study is open
- **Laboratory Normal Ranges**
  - Copy of normal ranges for all labs/tests included in protocol

...Regulatory File Contents...

- **Pharmaceutical Information**
  - Drug accountability including shipping and dispensing records
  - Sample of labels attached to investigational product containers
  - Decoding procedures (if not detailed in protocol)
  - Documentation may be kept in the pharmacy and a copy in the Regulatory file

…Regulatory File Contents

- **Training Records/Certificates/Inservices***
  - PI should ensure that there is adequate training for all staff participating in the conduct of the study.
  - Keep evidence of training such as:
    - Copy of human research training certification for all study staff
    - Additional training certification of study staff (e.g., chemo certification, phlebotomy, vital signs, etc.)
    - Sign-in sheets/copies of inservices conducted on a specific study
- **Blank Set of Case Report Forms**
- **Record of Retained Tissue or Fluid Samples**

** Not part of GCP E6(R2) but best practice to retain these records*

Regulatory File: Logs…

- **Delegation of Tasks Log/Signature Log**
  - List of all individuals who the PI delegates what types of activities to
  - Update as necessary
- **Subject Screening Log**
  - Patients who entered pre-trial screening period
    - Document why potential subjects were not included in study
- **Subject Enrollment Log**
  - Chronological enrollment of subjects

…Regulatory File: Logs

- **Site Visit/Monitoring Visit Log**
  - Document monitoring visits
  - Site staff will initial/verify that monitor was present on specific dates
  - For consecutive days, each day is entered separately

Notes to File…

- When something unusual happens in a clinical study
  - 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.
- Not a panacea for all things that have gone wrong
- Not a replacement for a reportable event to the IRB

…Notes to File

- A good note to file includes:
  - Study Name and IRB #
  - Subject ID (if applicable)
  - Purpose of the Note to File
  - Explanation, clarification, and/or description of corrective act
- Considered source documentation
- Must be signed and dated by either the person making the entry or the person reviewing and/or validating information the document contains

What should NOT be kept in a site/Investigator Regulatory File?

- Internal Audit Reports
- Study Budgets
- Study Contract Information

General Rules for Maintaining Regulatory Files…

- Make sure participant confidentiality is maintained
- Black out participant names and use subject numbers in reports
- File contents/organization need to be easily understood by someone who is not familiar with the study
- Develop naming conventions so that the contents of each file and document are apparent when viewing the labels

…General Rules for Maintaining Regulatory Files

- If using a binder/paper
  - Keep files in a secure location
    - Preferably locked cabinet
    - At a minimum locked office
  - File documents in reverse chronological order
  - Place in binder when received
    - Loose documents can fall out of the binder and get misplaced
  - Do not use binders to hold irrelevant papers

Centralization of Files

- If multiple studies have same regulatory documents, it is acceptable to file in one binder
- Place note to file in each study's regulatory file indicating location of centralized files
- Examples:
  - Laboratory Certifications and Normal Ranges
  - IRB Membership Lists/FWA
  - CVs
  - CITI training

Helpful Hints

- It's better to file documents into regulatory file as soon as they are received
- Be careful to file documents into the correct study's file
- Keep in mind the purpose of the file
  - Document compliance with GCP and regulatory requirements

Questions

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