WELCOME TO ONLINE TRAINING FOR CLINICAL RESEARCH COORDINATORS

ROLE OF THE RESEARCH COORDINATOR

Data Collection and Data Management Best Practices -21CFR Part 50

May 2016

Objectives

- Definitions used in Clinical Trial Data Collection
- Lifecycle of the Data Management Plan
- Source Document Tips and Tricks
- Electronic Documentation and Requirements of 21 CFR Part 11

Definitions Key to Research Documentation

1. **Source documents** are original records and certified copies of original records of clinical findings and observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. section 1.51 ICH E6 GCP
2. **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 for each trial subject (section 1.11 ICH E6 GCP) to capture essential source data about the subject for analysis to answer the hypothesis of a study.

Source Examples

- Original paper clinical visit note signed by a clinical professional (i.e. nurse, physician) at UCLA or in the community
- Electronic Medical Record (EMR) notes or reports scanned into EMR from outside medical offices
- Test results printed from an institutional EMR
- Pathology reports or procedures results
- Specific form created by Clinical Research Coordinator (CRC) for the study to record a mandatory process required by the protocol (i.e. PK sample shipment log, patient drug diary)

TIP: All Source must have a signature, original or electronic, by the person creating the source

Case Report Form (CRF) Examples

- Standardized and formatted document used in the same way for all subjects to transfer source data points into a database
- CRFs are provided by the study sponsor or created specifically for a P.I. initiated trial
- Best Practice: Designed or reviewed and signed off by the statistician who will be responsible for analysis
- Can be paper (but seen less today), excel spreadsheets or electronic CRMS (Best Practice)
- Abstraction from source documents is the only method for completing a CRF

Definitions Key to the Data Management Plan

1. **Data Management**

   Is the responsibility of the research staff and a host of other IT professionals related to collecting, entering, securing, and preserving data as a valuable, and reproducible resource for the outcome of the study.

2. **Data Integrity**

   Includes the development of policies and ethical practices for consistent procedures that properly manage the full data lifecycle needs for the outcome of a clinical trial. The principal investigator is the person responsible for data integrity, but must rely on a team of research professionals in IT and the research coordinators to uphold the policies.

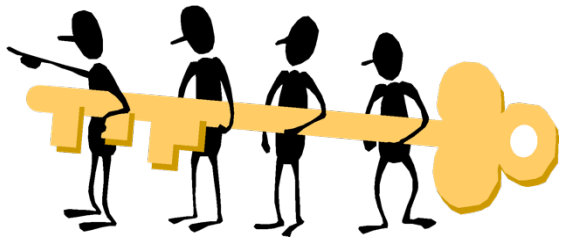
What does Data Integrity Look Like?

1. A relentless attention to detail and an impeccable ability to
   - Follow GCP guidelines, and
   - Carry out the protocol precisely as written.
2. A passion for
   - Accuracy
   - Completeness and
   - Timeliness of data entry and data corrections.

Who is Key in the Source to Data Lifecycle to Achieve Data Integrity?

It involves many different research members!

- Clinicians, Nurses and Clinical Research Coordinators (Site)
- Clinical Research Associates or CRA Monitors (Industry)
- Data Safety Committee (DSC) monitors
- Data Offices (Industry)
- Database Managers
- Biostatisticians (Site or Industry)
- Nurses, Doctors who manage safety offices for drug manufacturers (Industry)



*** The Investigator is the custodian of the Data Chain at the site level**

Data Management Plan Lifecycle

- ✓ Collecting
- ✓ Entering
- ✓ Reviewing
- ✓ Cleaning
- ✓ Coding (MedDRA, COSTART, ICD9 are common coding systems)
- ✓ Auditing
- ✓ Locking

Final product is a database containing data mirroring the source document ready for statistical analysis and publication or presentation.

Data Management Plan Best Practice; Let the Protocol Begin!

1. Protocol is approved
2. CRFs are created based on the protocol
3. Source Data is collected and entered and reviewed for accuracy in the CRF electronic system
4. Statistical Analysis – data is pulled for analysis
5. Principal Investigator reviews, signs off and publishes

Source Documentation
Important Differences to Responsibilities

- A Research Coordinator creates, collects and organizes Clinical Trial Documentation that is not medical or involving care of the subject.
- Medical Staff and Nursing Staff documents protocol required care or assessment of the subject's outcomes, adverse events, and compliance to study procedures.

Source Documentation

Tips and Tricks

When you need the subject to create the source…

- If the subject creates a source form, have them sign it since it becomes original documentation.
- Create a study calendar for the subject so that appointments and procedures occur on schedule.
- Monitor subject's study compliance and report and record protocol deviations from the data time points in the protocol.
- If subject diaries are created, find ways to ensure they are complete and collected on time at each visit.

Source Documentation

Tips and Tricks

- Obtain medical reports; create forms clinicians and nurses to use to help them comply with time points or assessments required per protocol.
- Create and maintain source documents; may use a copy of documents in a "research" chart for each subject.
- Meet and interview subject at each visit using forms that follow the protocol.
- Process and ship study specimens on time; complete logs and note deviations or missed samples.

Safe shipping certification for FAA regulations

49 CFR 172.700-704

Source Documentation

Tips and Tricks

Examples of 'must have' documentation

- Informed consent given and questions answered
- Eligibility criteria met for enrollment
- Discrepancy of study medication and returns of study medication
- Severity and causality/attribution of adverse events
- Deviations and violations of protocol

*Failure to capture this documentation will show up in audit reports against the site

Source Documentation

- ✓ If it is not documented it did not happen!
- ✓ ALCOA =Attributable-Legible-Contemporaneous-Original-Accurate
- ✓ No white out if paper
- ✓ Line through incorrect data, must be legible
- ✓ Date and initial changes and additions by appropriate research staff person
- ✓ Electronic Medical Records present security, and other legal challenges; know UCLA policies and requirements

***Always follow research documentation guidelines!**

The Study Coordinator, "Will it Ever Really Be PAPERLESS?"

Careful what you wish for!

If its Electronic Source, Now What?

Electronic Security is a very big problem!!

Never use portable disks, flash drives to transport or store patient source data!!!

- HIPAA violations come with serious fines
- HIPAA violations require lots of time to notify subjects
- Correcting electronic clinical information must be done in the electronic system and resigned by clinician on study team. It should not be done on a paper printout!
- Never sign or enter passwords for someone else
- Printouts if used for research patient files, must have a date/time stamp and show who printed the source document to make it verifiable as a copy
- Access to EMR by external staff from CRO or FDA requires an approval from Health Information Management

If its Electronic Source, Now What?

- Regulation 21 CFR 11(August 2003) provides criteria for acceptance by FDA of electronic records, electronic signatures
- FDA Guidance for Industry "Computerized Systems Used in Clinical Investigations"(May 2007) provides current thinking on records in electronic form that are used to create, modify, maintain, archive, retrieve, or transmit clinical data required; and ensuring confidence in the reliability, quality and integrity of electronic source data and source documentation.

If its Electronic Source, Now What?

- FDA recommendations on Internal Security Safeguards:

  Limited Access (individual account with log in access and unauthorized access per log-in attempts),

  Audit Trails (track all changes made to information entered in electronic system that documents activities related to the conduct of the trial),

  Date/Time Stamps (includes year, month, day, hour and minute) with limited access to changing this within the system.

- FDA recommends that computer education, training, and experience be documented.

Data Entry into Case Report Forms or CRFs

- **CRF is designed for entering data to the database consistently**
- **Delegated task from the PI to the research coordinator, but the PI remains responsible for the integrity of data.**
- Abstracted from the “source document” such as pharmacy records, clinical office notes
- Can be either paper or electronic and follows the same electronic security rules as the source documentation
- Designed by Sponsor or Cooperative group or study coordinator may design forms for investigator initiated trials.
- Changing or correcting entries follow the same rules as source: changes must show a date and identify of person, must be legible, never obliterate prior entry
- Data Entry must be accurate and complete!

Examples of Electronic Databases used in Clinical Trials

Must be compliant with
21CFR Part 11 FDA Electronic Records and Electronic signatures

CRMS is a **clinical research management system**. Creates, collects, stores, analyzes, allows monitoring and auditing for large amounts of data! It is a customizable software system used by the biotechnology and pharmaceutical industries to manage the large amounts of data involved with the operation of a clinical trial. Has CRFs and security built in with rules to maintain data integrity, security, and storage. Examples include:

- **UCLA: OnCore** - possesses the ability to manage most data items and
- **UCLA: webIRB** - Allows users to electronically submit research applications and other related forms to the IRB.
- **Industry sponsors** - Inform, Phase Forward , Medidata Rave

Case Report Form

- ✓ Only collect and enter data required for analysis
  Too much data = *noise* which interferes with analysis; use of a statistician as part of the data management plan will manage the data!
- ✓ Code entries whenever possible to minimize text which cannot be analyzed in statistical programs.
- ✓ Do not collect the same variable more than once so errors can be minimized.
- ✓ Double data entry is a process used to catch errors quickly because usually two people entering data do not make the exact same mistake. Clean data is the best data!

Case Report Form

Tips and Tricks

- ✓ All forms include should use a header to identify protocol and form name since the subject code rather than subject PHI should be used.
- ✓ Personal identifiers removed using IDs: Patient ID, and Site ID
- ✓ Check with investigator before choosing a data dictionary term when the symptom written in the source is not available in the database.
- ✓ ASK before entry! Before you enter any data that you are unsure about….ASK your investigator and ASK your monitor

Takeaways…

- Data integrity is everyone's responsibility but the Principal Investigator is the custodian at the site level.
- The role of the Clinical Research Coordinator is the assure source documentation and data abstraction and entry are being done at the protocol specified time-points.
- Electronic data, whether source in the electronic medical record or the pure data in the case report form, holds additional security issues.