

Clinical and Translational  
Science Institute / **CTSI**  
at the University of California, San Francisco



Welcome to Online Training for  
Clinical Research Coordinators

# ROLE OF THE RESEARCH COORDINATOR

## Data Collection and Data Management Best Practices 21CFR Part 11



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# 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 UCSF 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 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 CTMS (Best Practice)
- Abstraction from source documents is the only method for



# 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?

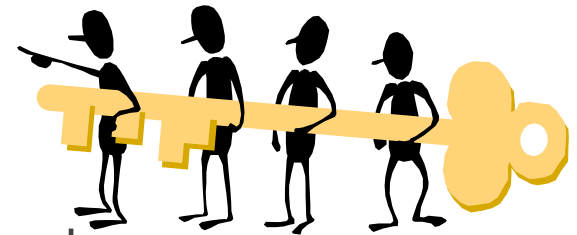
1. A relentless attention to detail and an impeccable ability to
  - Follow GCP guidelines, and
  - Carry out the protocol precisely as written.
2. A passion for
  - Accuracy,
  - Completeness, and
  - Timeliness of data entry and data corrections.



# 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**



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# 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 UCSF regulations

**\*Always follow research documentation guidelines!**



# The Study Coordinator, “Will it Ever Really Be PAPERLESS?”



Careful what you wish for!



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# 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**

CTMS is a **clinical trial 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:

- **UCSF: OnCore** - possesses the ability to manage most data items and
- **UCSF: iRIS** - Allows users to electronically submit research applications and other related forms to their institute's review board(s)
- **Industry sponsors** - Inform, Phase Forward , Medidata Rave



# Case Report Form (CRF)

## Tips and Tricks

- ✓ 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.

