Data Capture Methods
CRF design
Data entry

Module 8 Topic 3

Definition of Clinical Data Capture

Collection of clinically significant data by the Investigator/s for clinical trials on behalf of the Sponsor in a sequential manner (per protocol) to process the same and generate reports at a later stage for submissions to regulatory authorities for various purposes

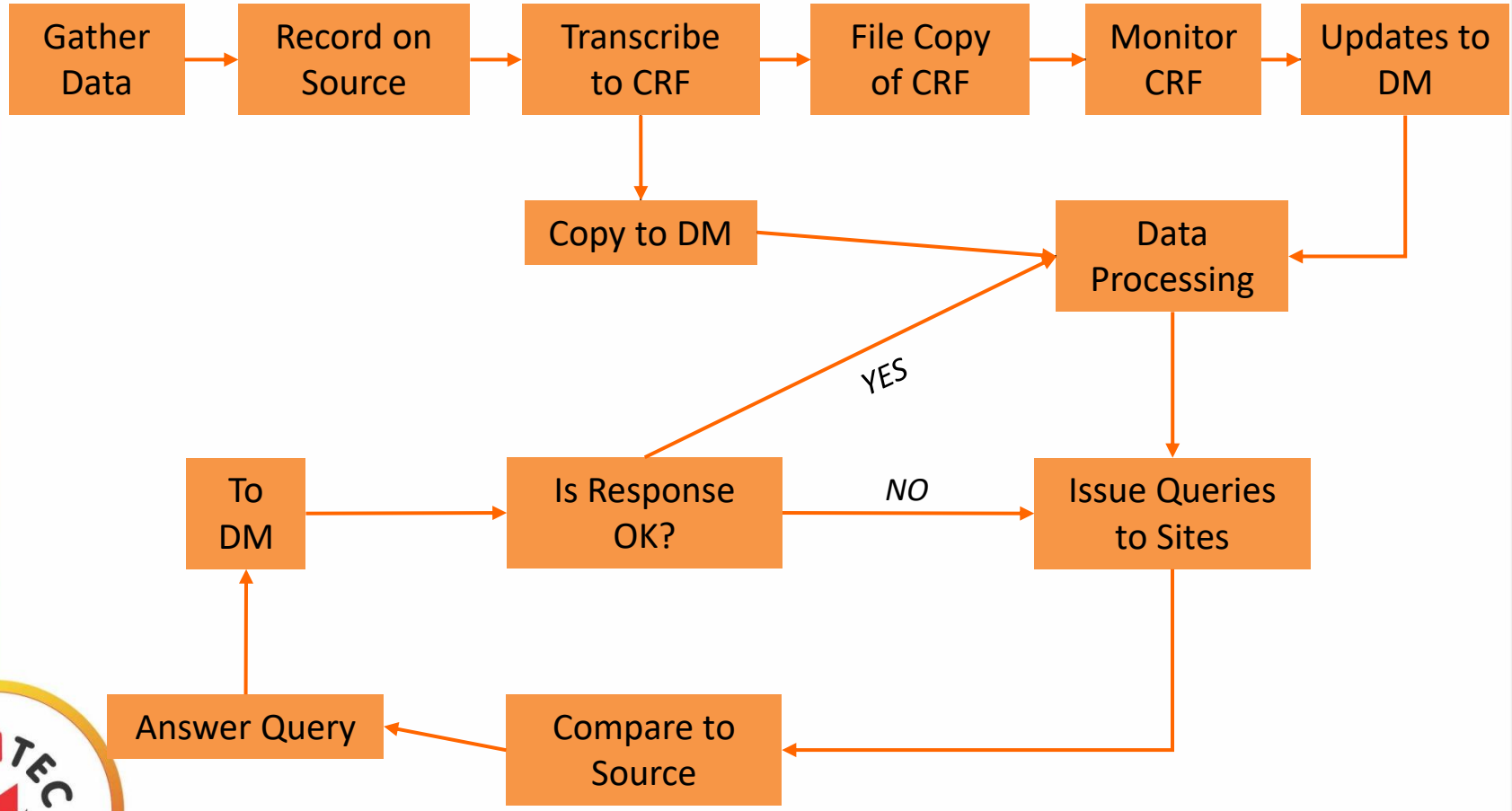
Clinical Data Capture

- Procedures for gathering and recording data from or related to subjects in the study
- Paper based OR Electronic Data Capture (EDC)
- Promise of increased efficiency has led to increasing movement toward implementation of the electronic medical record and to computerised automation in general

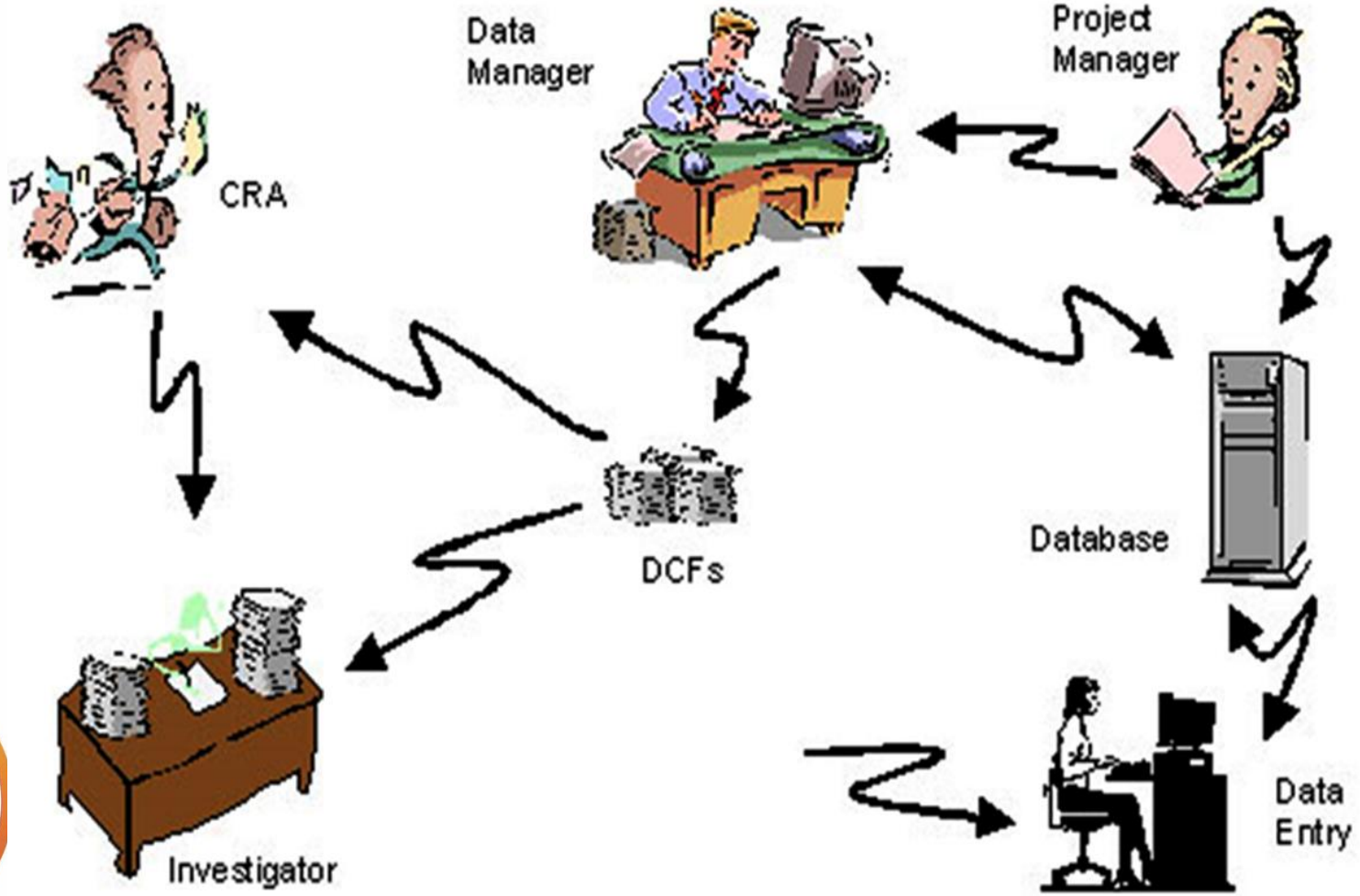
Paper Based Data Capture

- Most widely used form of data capture
- Traditional paper Case Report Forms (CRFs)
  - Manual entry by site personnel on three-part NCR paper CRFs
  - 1 copy retained at investigator site, 2 copies sent to Sponsor or CRO's Data Management department
- Easy to enter data
- Requires simple training
- Logistically patient's bedside may not be the right place for a computer to enter data

Paper CRF Process



Data Flow In A Traditional Paper-based Clinical Trial:



Draw Backs of Paper CRF

- Storage problem
- Time consuming
- Cost of printing and distribution/ Imaging
- Lack of real-time reporting
- Increasing pressure on sponsors to get drugs into market faster
- Confidentiality and Security

Electronic Data Capture (EDC)

- Capability to collect data electronically
- Also known as Remote Data Entry (RDE)
- Online and offline
- Becoming more common than paper technology

Definition of EDC by the Clinical Data Interchange Standards Consortium (CDISC):

- "Collecting or acquiring data as a permanent electronic record with or without a human interface (eg., using data collection systems or applications that are modem-based, web-based, optical mark/character recognition, or involve audio text, interactive voice response, graphical interfaces, clinical laboratory interfaces, or touch screens).

Note: 'Permanent' in the context of these definitions implies that any changes made to the electronic data are recorded via an audit trail."

EDC Tools

- Internet
- Interactive Voice Response (IVR)
- Pen Tablet
- Personal Digital Assistant
- Fax
- Image Recognition Technology (OCR & OMR)
- eCRF

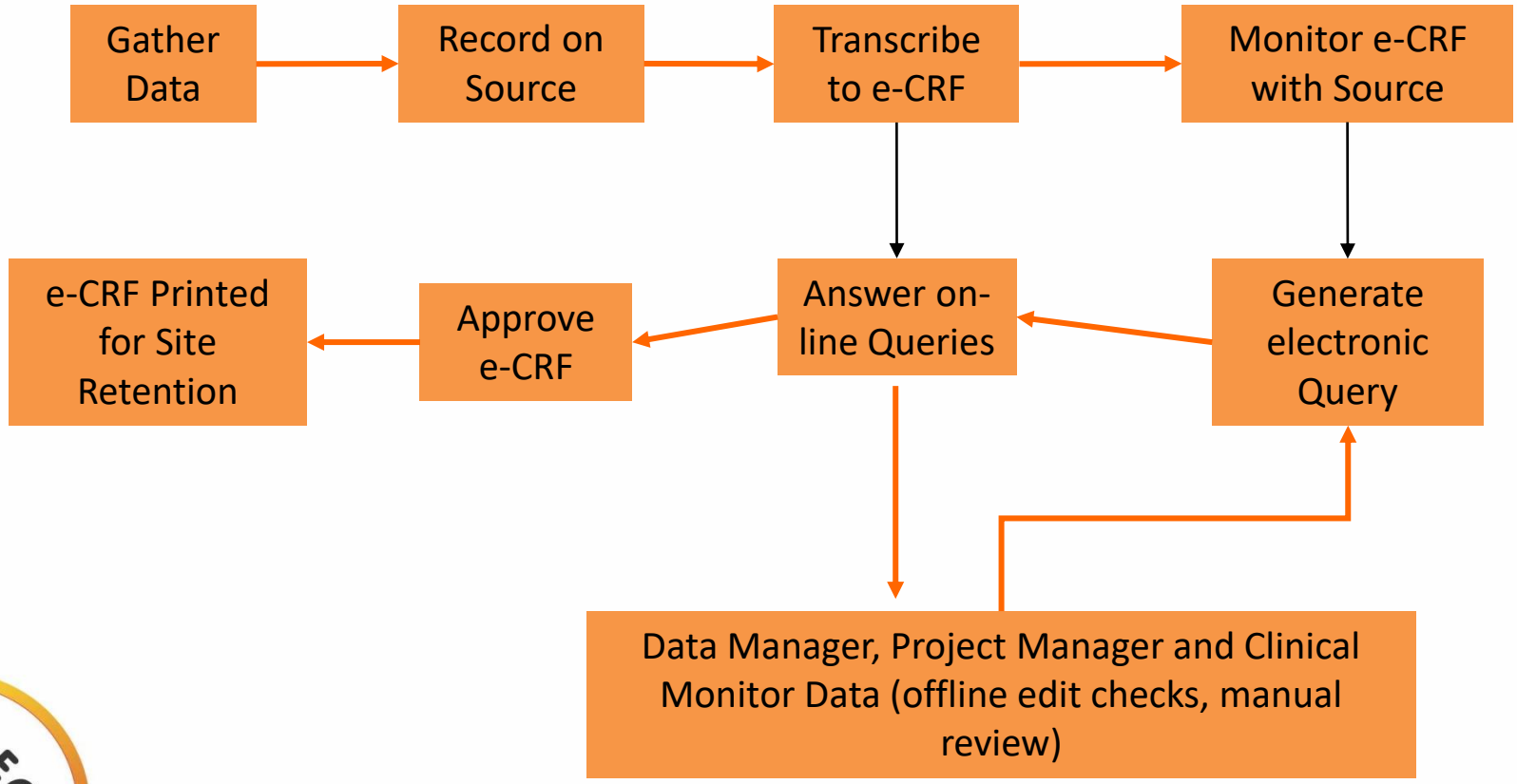
eCRF

- Direct entry into eCRFs that have some form of in-built real-time data validation checks. **Updates to data done electronically**
- **Transmission of data to sponsor accelerated**
- Faster and more active management of the data gathering and processing workflow
- Ensures “cleaner data faster”

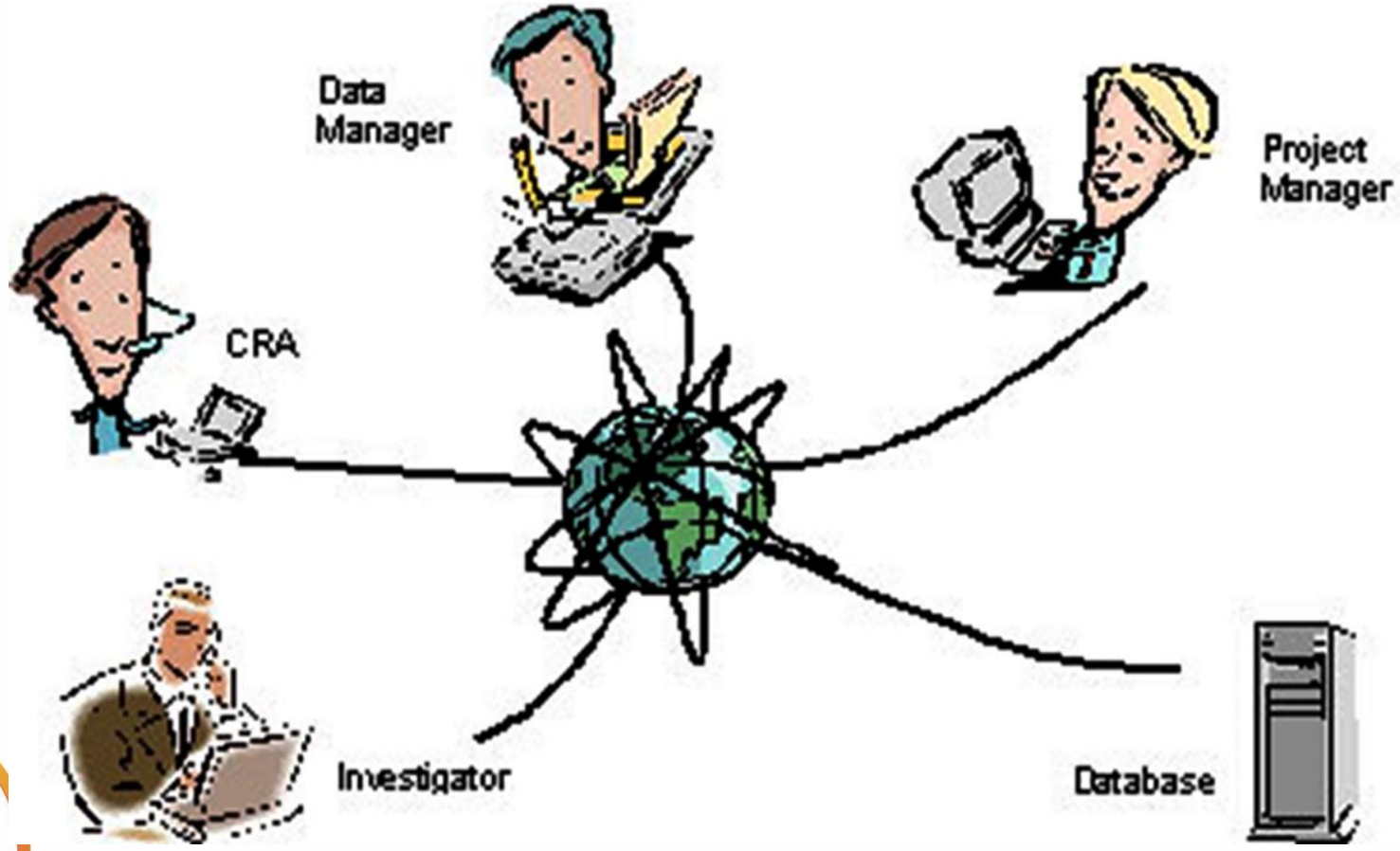
eCRF (contd)

- User interface to be designed with user characteristics in mind
- Validation inputs to be taken into account during initial designing
- Integration of EDC with other corporate systems to be included in designs from the start, as well as information messaging and workflows

eCRF (contd)


Gather Data
Record on Source
Transcribe to e-CRF
Monitor e-CRF with Source
e-CRF Printed for Site Retention
Approve e-CRF
Answer on-line Queries
Generate electronic Query
Data Manager, Project Manager and Clinical Monitor Data (offline edit checks, manual review)

Data flow in an eCRF EDC clinical trial



Advantages of eCRF Over Paper CRF

- Automated data edit checks alert the site to possible errors in data entry
- Faster correction of issues and immediate site education. Hence cost saving
- Immediate viewing by sponsor to review and analyse the data and provide online feedback to the site.
- Shortens time between ‘last patient last visit’ and ‘database lock’

Advantages of eCRF

- Project Manager: access to real-time project metrics
- Clinical Monitoring Staff: less time spent in site visits
- Investigator Sites: less query resolution and less storage issue
- Data Management: eradication of double data entry and faster turn around

Limitations of eCRF

- Resistance to change
- Integration of multiple systems and groups
- Indecision and fear among Sponsors

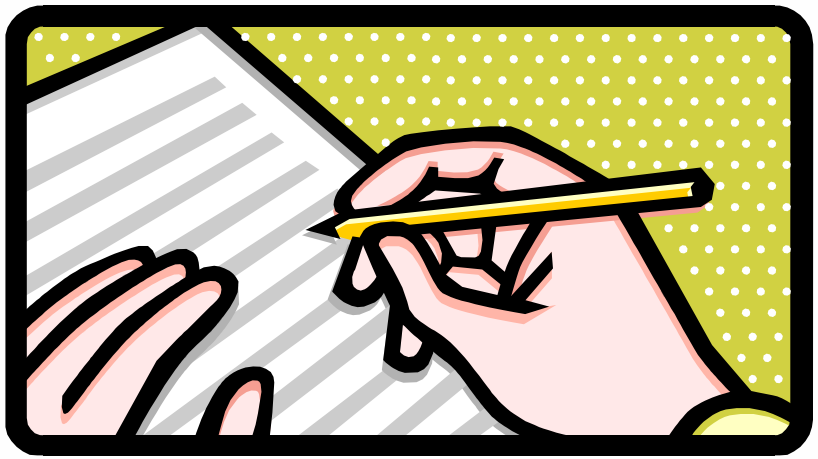
Case Report Form

Design and Format

Definition

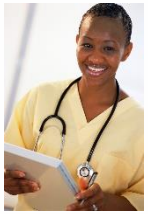
A **printed, optical, or electronic** document designed to record all of the **protocol required** information to be reported to the sponsor on each trial subject

GCP (consolidated Guideline) Section 1.11



CRF

- The forms used to record the **patient's data** obtained during the clinical study are collectively called as CRF



- CRFs are
  - Designed by the sponsor
  - Completed by the Investigators
  - Reviewed By the Monitor
  - Entered by the Data Management team
  - Analyzed by the Biostatistician

Instructions for CRF Designing

- Use inputs from the study team
- Request minimal free text responses
- Record dates to help trace source data
- There should be one CRF per subject
- Any parameter that will not be analyzed should not be included

CRF Responsibilities

Project Manager	Leads, manages, works with statistician, provides input on design, reviews
Investigator	Assures correct entering of CRFs
Monitor	Checks for accuracy and consistency
Data Manager	Reviews and edits
Statistician	Gives inputs, ensure CRF and database tally

Accurate Documentation

- Provides basis for safety and efficacy evaluation of the drug
- Documents protocol adherence and protection of human subjects
- Validates data integrity and analysis

Contents of the CRF

- Must be protocol driven
- Must contain sections on
  - Study Number, Center Code, Patient Number
  - Name, signature of Investigator
  - Version, Date, Page numbers
  - Emergency Numbers
  - Instructions for filling the CRF
  - Study Flow Chart
  - Inclusion /Non-inclusion criteria
  - Demography of Patients
  - Medical History of Patients
  - Concomitant Medications/ Previous therapy
  - Current Illness (Signs and Symptoms/ Diagnosis)

Contents of the CRF (contd)

- Must contain sections on (contd)
  - Study Medication dosing details
  - General Examination
  - Laboratory Examination
  - Special Examination
  - Adverse Event Reporting
  - Serious Adverse Event Reporting
  - Compliance Check
  - Efficacy Parameters
  - Safety Parameters
  - Global Evaluation of Efficacy and Tolerability
  - End of Study Information

Inclusion Criteria

Please Check all statements and tick (✓) the appropriate box

- Morning stiffeness in and around joints lasting 1 hour

  Y ☐ N ☐

If the answer is “No” to any of the above, please do not enroll the patient

Concomitant Illness and Medications

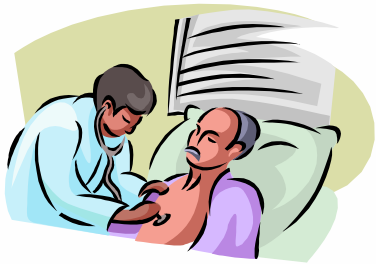
Condition	Name of The Drug (Generic)	Dosage Strength/ Frequency	Started on	Remarks
Hypertension	Atenolol	50mg OD	Date	

STUDY MEDICATION DOSING DETAILS

- Treatment A/B
- Dose: ____mg
- Frequency: OD/BID

General Examination

- VITAL SIGNS
  - Body Temperature
  - Pulse Rate
  - Blood Pressure



Laboratory Examination

- Complete Blood Count: **Hb, WBC, RBC, ESR, Platelets etc.**
- Enzymes: **Alkaline phosphatase, SGPT, SGOT etc.**
- Blood Sugar: **Fasting, PP, HbA1C**
- Urine Analysis
- ECG findings
- Other Investigations

Normal Lab values must be given either in the CRF or separately

Special Examination

- Depends on the type of the study
  - For Pain, pain VAS score is analysed
  - For Inflammation, swelling, redness, local temperature, pain are analysed
  - For RA, HAQ score is determined
  - For hypertension, DBP, SBP average of 3-6 readings are taken into consideration

Adverse Event Reporting

- Did the patient experience any of the following?

Event	**Yes / No**	**Severity** Mild/Moderate /Severe	**Treatment** If given Drug, Dose	**Outcome** Continued/ resolved
Nausea				
Abdominal Discomfort				

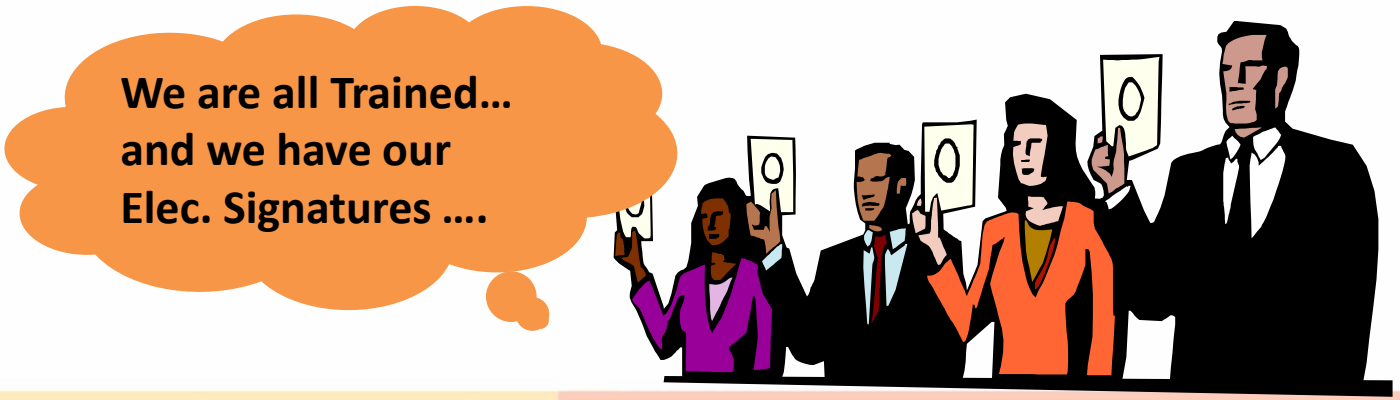
Data Entry Methods

Entering Data

- Accuracy of transcribing data
- Dealing with problem data
- Making edits & changing data
- Quality control

Before Starting with Data Entry Process

- Understanding 21 CFR Part 11, that is, Code of Federal Regulations part 11 chapter 21
- FDA defines that persons handling clinical data have to be sufficiently trained & need to have electronic signatures of their own
- Therefore, each person will have electronic signature as part of 21 CFR Part 11 compliance



Audit Trail & 21 CFR Part 11

Audit Trail means ...

- “Record of Activities”
- Data entered, deleted, altered, updated etc.
- E-signature help us identify who did what?

FDA CFR Part 11

Food and Drug Administration

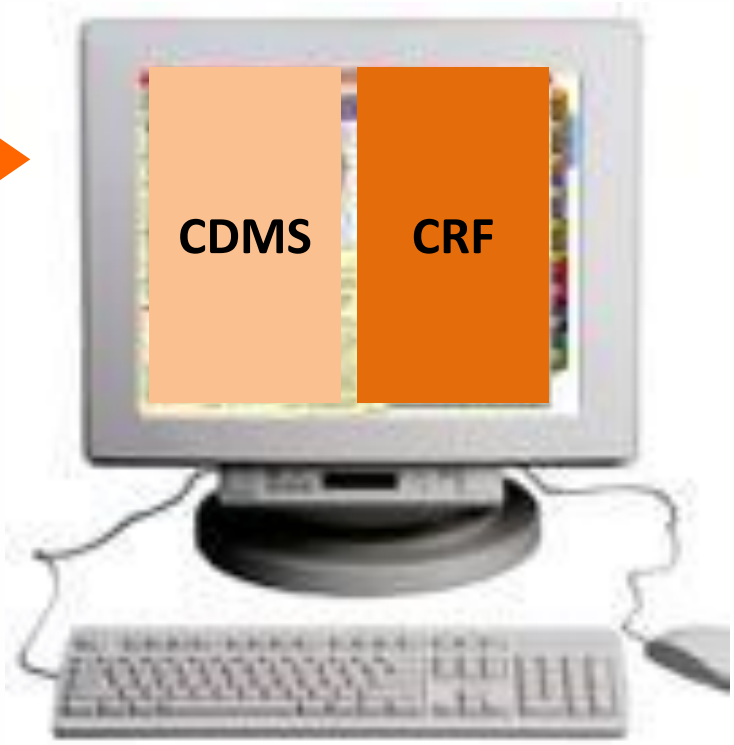
Das muss für den exportierenden Verpackungsmaschinenhersteller

Data Entry Screen

- Understanding Data Entry

Left Side
CDMS Screen

Right Side
Scanned CRF Image

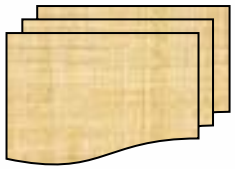


Types of Data Entry

- Double Entry
- Single Entry

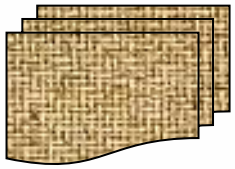
Double Data Entry

- DEO selects work items (consisting of CRF pages)



Work Item

- After selecting work item, completes data entry of all CRFs & releases work item for next step



Release Work Item

Data Entry

First Pass Data Entry

- Refers to data being entered to database for first time
- DEO enters all data of each document & releases work item

Second Pass Data Entry

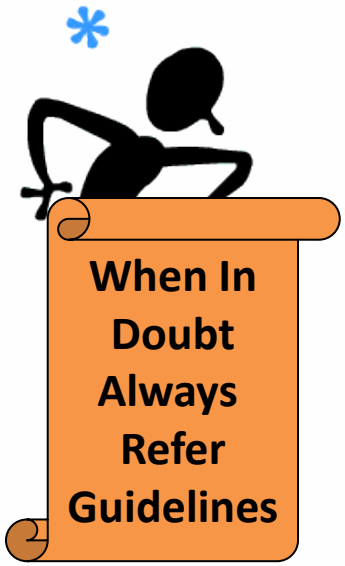
- Second pass entry done by another DEO, following first entry
- This becomes first quality check in CDM process
- Both DEO & system contribute to this first quality check in CDM process
- System gives an alert if second pass enters anything different from first pass
- Correct value is confirmed & entered

DE Guidelines

Best Practices of Data Entry

- DEOs should develop habit of referring data entry guidelines when in doubt

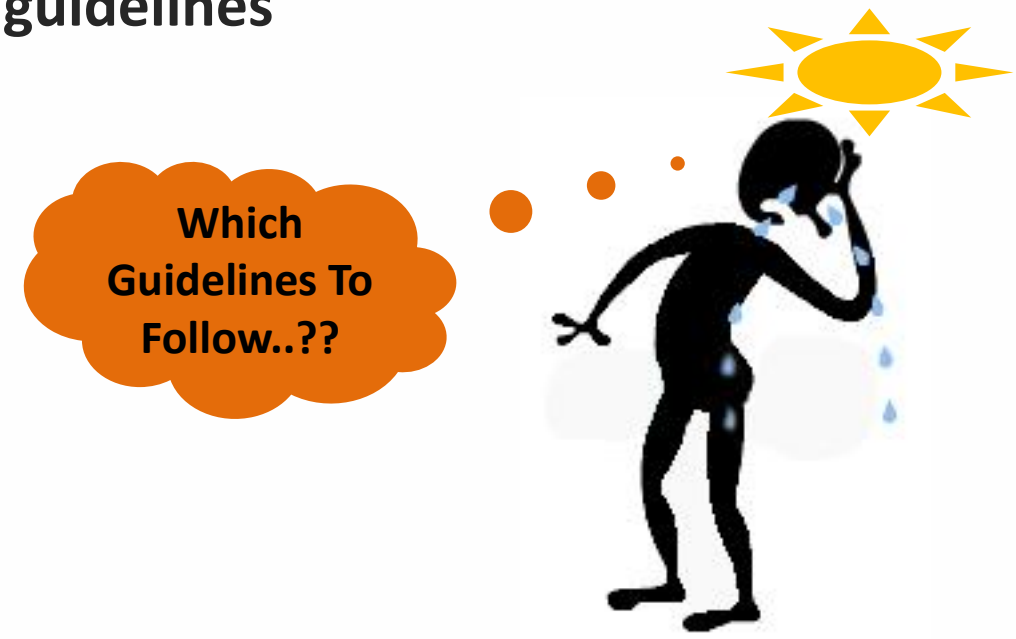
- If still unclear, they can raise a comment or flag for further review of data



Standard & Project Specific Guidelines: Which One to Follow ?

- DEOs are required to follow numerous guidelines

- They should be aware that always **“project specific guidelines supercedes standard guidelines”**



QA/QC

- Quality Assurance is a process
- Quality Control is a check of process
- Accuracy of data entry checked by auditing data stored in database against CRF
- Ongoing internal and external audits
- Error Rate: “number of errors / number of fields on CRF or Database”
- Acceptable error rates – client specific