



Clinical Data Management Overview

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Learning Objectives



- ❖ Overview of Process Related to Clinical Data
- ❖ Principles of Data Management
- ❖ Data Management Activities
- ❖ Changes Happening Now and in the Future

Functions/Roles at Sponsor/CRO Related to Clinical Data



- ❖ Project Leader (leads cross-functional team for each drug project)
- ❖ MD or Clinical Scientist
- ❖ Statistician
- ❖ SAS Programmer
- ❖ Clinical Pharmacokineticist
- ❖ Clinical Research Associate/Monitor
- ❖ **Clinical Data Manager**
- ❖ Clinical Pharmacovigilance
- ❖ Regulatory Affairs
- ❖ Regulatory Operations
- ❖ Clinical Quality Assurance
- ❖ Medical Writing
- ❖ Information Management/Information Technology

Effective Clinical Data Managers



Task

Competencies

Understanding – protocol, documentation, SOPs, regulations, roles and responsibilities	Attention to detail; organisational skills e.g. understand instructions
Execution of tasks – discrepancy management, data review, UAT, data locking	Attention to detail; personal organisation e.g. deliver on time, planning; software skills
Effective communication – with study team, monitors, study data manager	Good written and verbal communication skills; influence; interpersonal skills
Issue identification	Attention to detail; problem solving; tenacious
Process improvement identification	Attention to detail; strategic thinking; displays initiative

Examples - variety of available jobs / pathways

Statistical Programming

Data Management

Clinical Operations

Programming Mgr

Program Data Leader

Studies Leader

Snr Programmer

Study Data Manager

Operations Manager

Programmer

Data Manager / Programmer

Studies Associate

Internal Talent Pool

External
Talent Pool



Clinical Trial Phases of Drug Development Process (1 of 3)

- ❖ The drug development process requires many resources. Before a new drug is marketed, it must undergo **extensive testing** and be approved by regulatory agencies in the countries where it will be marketed. Human clinical trials generally consist of **four phases**, **starting** on a **small** scale to assess **safety** and then **expanding** to **larger** trials to test **efficacy**.
- ❖ **Phase I**
 - Phase I trials involve testing the drug on a **limited number** of **healthy individuals**, typically 20 to 80 people, to determine the drug's **basic safety** and **pharmacological data**. This phase of the drug development process lasts an average of six months to one year.
- ❖ **Phase II**
 - Phase II trials involve testing a **small number** of volunteer **patients**, typically 100 to 200 people who suffer from the **targeted disease**, to determine the drug's **effectiveness** and **dose response** relationship. This phase of the drug development process lasts an average of one to two years.

Clinical Trial Phases of Drug Development Process (2 of 3)

❖ Phases IIIa-b

- Phase IIIa trials involve testing **large numbers of patients**, typically several hundred to several thousand persons, to **verify efficacy** on a large scale as well as **safety**. Phase IIIa trials are focused on **regulatory approval** issues and involve numerous sites and generally last two to three years. After the successful completion of Phase IIIa, the sponsor of a new drug submits a **registration dossier** containing all pre-clinical, pharmacologic, efficacy, and safety data; information about the drug's composition; and the sponsor's plans for producing, packaging and labeling the drug. The regulatory review process can take up to

Clinical Trial Phases of Drug Development Process (3 of 3)



❖ Phase IV

- Phase IV trials begin **after regulatory approval** and typically are used to prove safety and efficacy in **new indications** (uses); to test new dosage strengths and formulations, e.g., a sustained release capsule or a flavored solution for children; to confirm certain extra clinical benefits such as **cost-effectiveness** or **improved quality of life**; and to collect and analyze **long-term safety data** on patients treated with the drug in **normal practice**.

Overview of Process Related to Clinical Data

(1 of 3)

- ❖ Develop Clinical Development Plan for each Drug Project
- ❖ Develop Protocol
- ❖ Select Investigators
- ❖ Develop (e)Case Report Forms (and system)
- ❖ Design and implement Edit Checks
- ❖ Select vendors (e.g., laboratory) and test data interface
- ❖ Train project team
- ❖ Prepare investigator's site and people



Overview of Process Related to Clinical Data

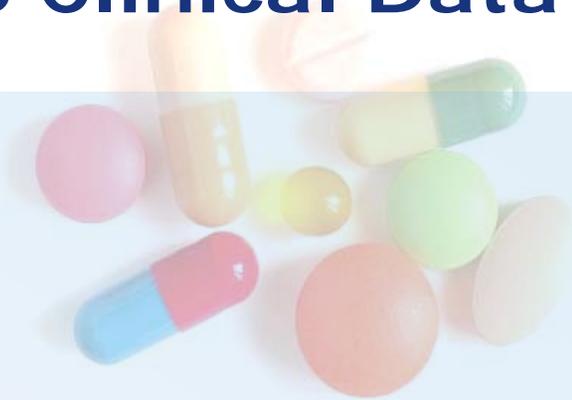
(2 of 3)



- ❖ Collect data (in blinded fashion for double-blind studies)
 - Monitoring
 - Data review and coding
 - Query generation and resolution
 - Merge vendor data, generate more queries
- ❖ Handling of Serious Adverse Events by Sponsor's Pharmacovigilance personnel
- ❖ Unblinded review by Independent Data Safety Monitoring Board, if needed
- ❖ Quality Assurance Audits by Sponsor

Overview of Process Related to Clinical Data

(3 of 3)



- ❖ Determine patient acceptability
- ❖ Lock data base then break the blind
- ❖ Deliver to Statisticians/SAS Programmers
- ❖ Finalize database documentation
- ❖ Write clinical study report
- ❖ Create integrated database for safety and efficacy when needed
- ❖ Prepare e-submission CRFs, electronic Case Report Tabulations with documentation for NDA submission

Collection of Clinical Data



- ❖ Investigator/staff record observations/data onto source documents
 - Source document: where data is first recorded or a certified copy of that
- ❖ Data is transcribed by Investigator staff onto Case Report Form (CRF) or entered into electronic Case Report Form (eCRF)
- ❖ Vendor data usually transmitted electronically to sponsor database (e.g. lab data)
- ❖ CRF data entered/transferred into sponsor database

The Investigator

The heart of the clinical trial



Investigator Responsibilities

21 CFR Part 312.62b

Investigator must *maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation.*



Two Worlds of Clinical Data Management (CDM)



❖ Paper world

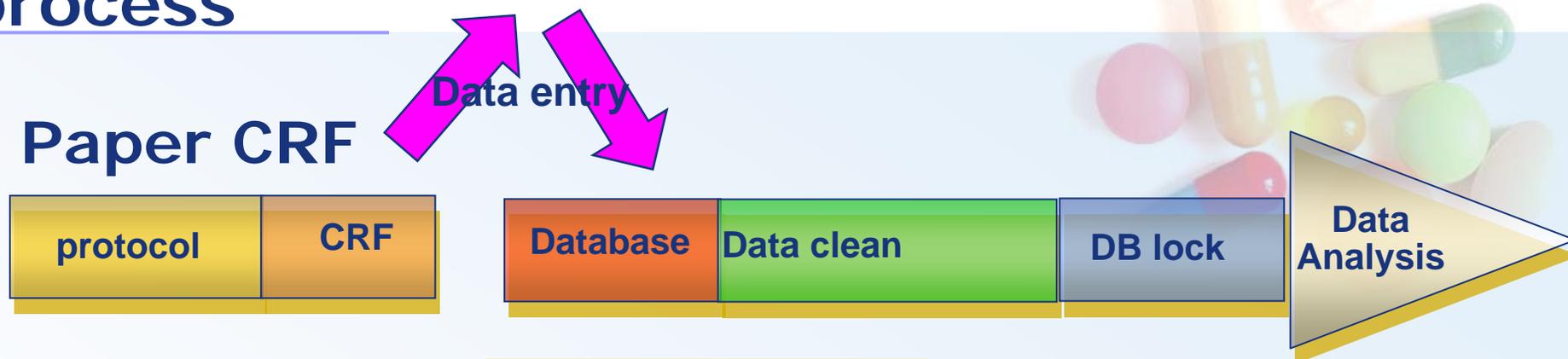
- Source data in pt. chart
- CRFs completed at site and sent to Sponsor
- Double Data Entry
- Queries
- Data Correction Forms (DCF) record changes
- Database matches CRF and DCFs

❖ Electronic Data Capture

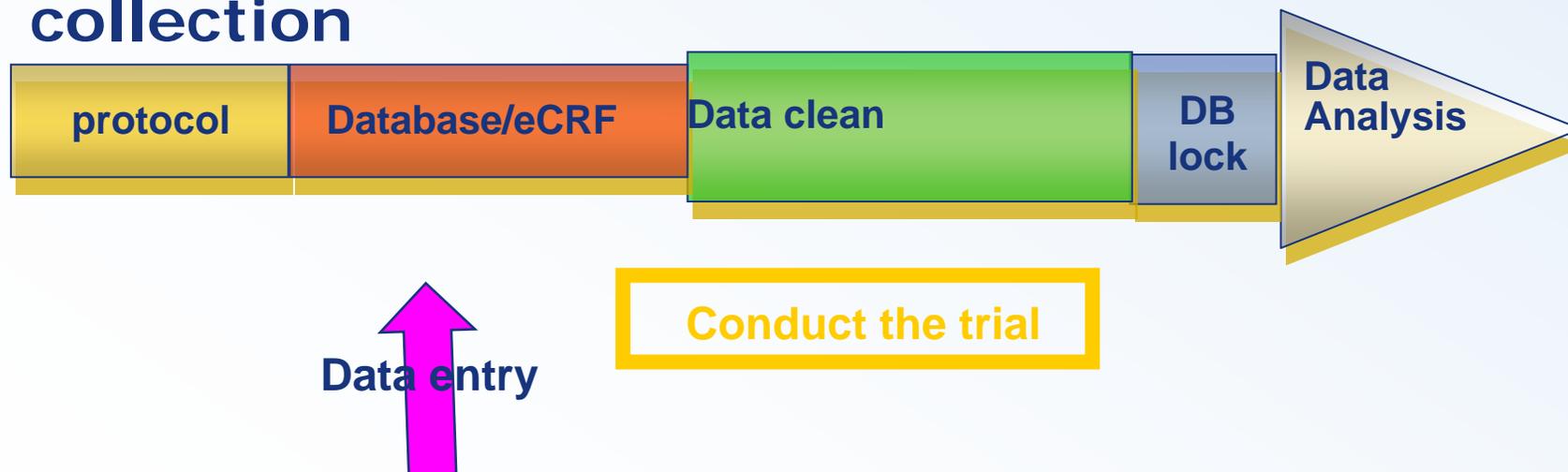
- Source data in pt. chart
- Data entered at site with edit checks upon entry
- Queries
- Data corrected in system
- eCRFs created from system
- Database matches eCRF

Difference between e-process and paper process

Paper CRF



Electronic data collection



Learning Objectives



- ❖ Overview of Process Related to Clinical Data
- ❖ **Principles of Data Management**
- ❖ Data Management Activities
- ❖ Changes Happening Now and in the Future

Principles of Clinical Data Management (1 of 3)



- ❖ Sponsor database *contains* all data required in the protocol to document the safety and efficacy of our products
- ❖ Sponsor database *matches* the (e)CRFs on file in Central Records and includes other data loaded electronically (i.e., lab, ECG, DXA, etc.)
- ❖ Goal is to get data *clean* and complete according to the data cleaning strategy for each study
- ❖ *Comply* with relevant laws, regulations and guidelines, including 21 CFR Part 11, HIPAA, GCP, ICH, Guidance on Computerized Systems Used in Clinical Trials, Guidance on electronic submission requirements, CDISC standards for SDTM.

Principles of Clinical Data Management (2 of 3)



- ❖ Work to meet project *timelines* agreed by Clinical Execution Teams and Submission Teams without violating other principles
- ❖ Use *Standard* Work Processes, follow our Standard Operating Procedures (SOPs) and agree/document exceptions prospectively
- ❖ Make sure data can be readily *analyzed* and combined across studies within a drug product
 - Use standard data elements, e.g., forms, items, code lists, events, derivations, and procedures.
 - Support the development of drugs/products, not only each protocol, so each protocol for a drug/product is handled in a similar way: same decisions, same data rules/data items/codes where possible/reasonable

Principles of Clinical Data Management (3 of 3)

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- ❖ Protect the blinding of all personnel involved in study and submission (*Privacy*)
 - ❖ In general new data and/or changes received after the database is unblinded are not included in the clinical database
 - An exception is bioanalytical data that are planned to come in after unblinding.
 - The decision to unlock a database to accept “post finalization data” is made by the clinical execution team and is not taken lightly because it calls into question the integrity of the blinding.
 - Changes should only be made if they alter the primary conclusion of the study, are so numerous that they call into question the quality of the database, or are important new data affecting safety

Learning Objectives



- ❖ Overview of Process Related to Clinical Data
- ❖ Principles of Data Management
- ❖ **Data Management Activities**
- ❖ Changes Happening Now and in the Future

Activities of Data Management



- ❖ Study set-up and planning
- ❖ Blinded Review and Coding of Investigator's Data
- ❖ Load and Review of Vendor Data
- ❖ Database lock activities
- ❖ Database documentation
- ❖ Prepare esub (e)CRFs and datasets for NDA submissions

Study Set-Up and Planning Activities

- ❖ Design and implement (e)CRFs using data standards
- ❖ Develop (e)CRF completion guidelines
- ❖ Identify critical variables
- ❖ Establish specifications for edit checks
- ❖ Program and test edit checks
- ❖ Identify and select data vendors (labs, ECG, DEXA, etc.)
- ❖ Set-up and test data exchange with vendors
- ❖ Set-up and validate internal database, if separate
- ❖ Provision sites for EDC, if needed
- ❖ Train users on (e)CRF completion (and EDC)
- ❖ Set-up EDC hotline/help desk, if needed
- ❖ Agree schedule for database lock



Final Database Lock Activities



- ❖ Add any data that would unblind the study
- ❖ Merge randomization code to assign treatment groups
- ❖ Flag database records as being locked
- ❖ Deliver database (as SAS datasets) to biostatistics and clinical pharmacokinetics

Database Documentation (1 of 2)



- ❖ Data Management Plan
 - Including critical variables
 - Specifications for edit checks
- ❖ Database Documentation
- ❖ Database Validation:
 - User Acceptance Testing
 - Post Production Changes
- ❖ Site instructions for completing (e)CRF
- ❖ Data Entry, for paper study
 - Annotated CRF
 - Data Entry Instructions

Database Documentation (2 of 2)



- ❖ Vendor Data
 - Load Specifications
 - Data Load Execution
- ❖ Randomization documentation
- ❖ Quality Control Check Documentation
- ❖ Exceptions to SOPs
- ❖ Database Finalization
 - Critical Variable Summary
 - Interim Analysis Documentation
 - Database Finalization Documentation
 - Database Post Finalization Documentation
- ❖ Post-finalization Data Base Quality Review Audits
- ❖ EDC Helpdesk Documentation
- ❖ Other Database Correspondence

Learning Objectives



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Changes happening now and in the future

(1 of 2)

- ❖ Paper → EDC
- ❖ Electronic Patient Recorded Outcomes (ePROs)
 - PDAs, IVRS, Tablets, Laptops, Web Collection
- ❖ Increase in Technology
 - Patient recruitment
 - Data measurement
 - Data collection
 - Communication
 - Data review
- ❖ Adaptive design studies



Changes happening now and in the future

(2 of 2)

- ❖ Globalization of Clinical Research
 - Western Europe → Eastern Europe
 - India and Asia
 - South America
 - South Africa
- ❖ Globalization of Submissions
- ❖ New business models
 - Outsourcing
 - Off-shoring
 - Strategic Alliances (preferred providers)
 - Partnership (alliance of 2 pharma companies)



The 2nd Clinical Data Management Training



Thank You !