



Clinical Data Management

-An Introduction

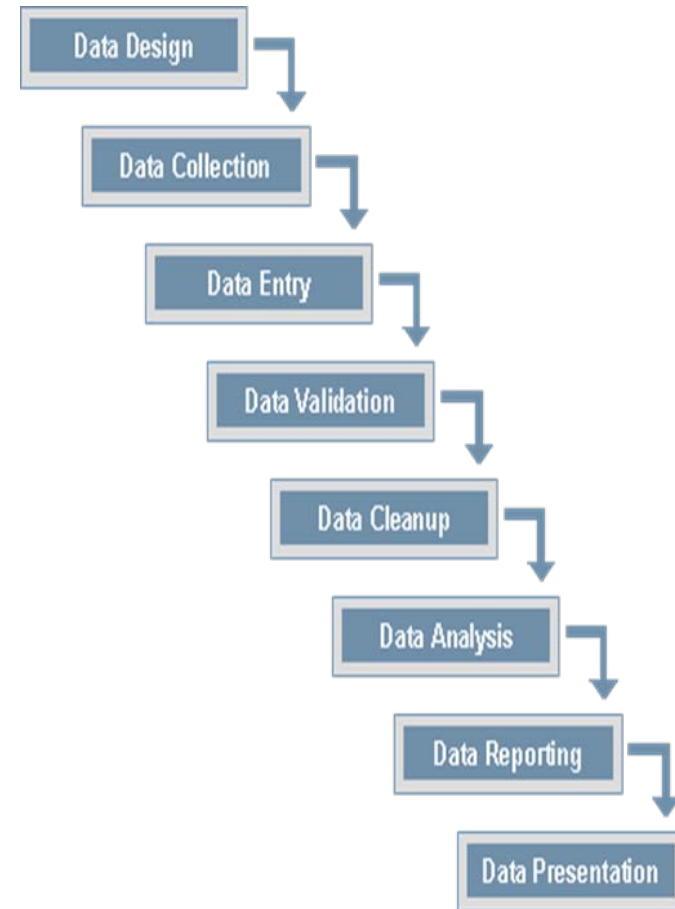
What is Clinical Data Management

Clinical **D**ata **M**anagement is involved in all aspects of processing the clinical data, working with a range of computer applications, database systems to support collection, cleaning and management of subject or trial data.



CLINICAL TRIAL DATA

- Clinical Data Management is the **collection, integration and validation** of clinical trial data
- During the clinical trial, the **investigators** collect data on the patients' health for a defined time period. This data is sent to the trial **sponsor**, who then analyzes the pooled data using statistical analysis.



Why CDM

- Review & approval of new drugs by Regulatory Agencies is dependent upon a trust that clinical trials data presented are of sufficient integrity to ensure confidence in results & conclusions presented by pharma company
- Important to obtaining that trust is adherence to quality standards & practices
- Hence companies must assure that all staff involved in the clinical research are trained & qualified to perform data management tasks



Key Members

The Key members involved in Data Management

- Project Manager /Data Manager
- Database Administrator
- Database Programmer / Developer
- Clinical Data Associate

THE BIGGER PICTURE



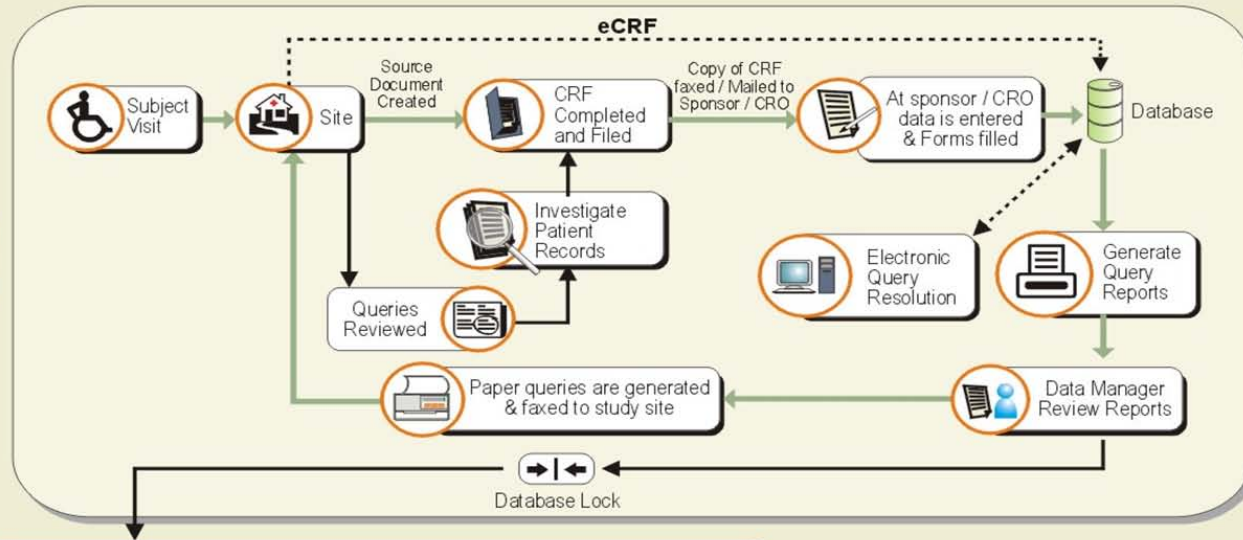
CLINICAL TRIAL OVERVIEW

Planning

Activity : • Create Protocol Document • Approve & Sign Off

Design / Development

Activity : • DB Setup • Form Design • Edit Checks • Validation



Data Management / Review

Analysis

• Statistical Planning • Programming • Medical Writing

Filing

Submission Co-ordination → QA → Review → Create Submission → Regulatory Authority

Multidisciplinary Teams in Clinical Trials

1. Clinical Investigator
2. Site coordinator
3. Trial Pharmacists
4. Biostatistician
5. Lab Coordinator
6. Project manager
7. Clinical Research Manager/Associate
8. Monitor
9. Ethics committee
10. Regulatory affairs
- 11. Clinical Data Management**
12. Pharmacovigilance
13. IT/IS personnel
14. Clinical supply
15. Auditor/Compliance

Responsibilities of CDM

Study Setup

- CRF design and development (paper/e-CRF)
- Database build and testing
- Edit Checks preparation and testing

Study Conduct

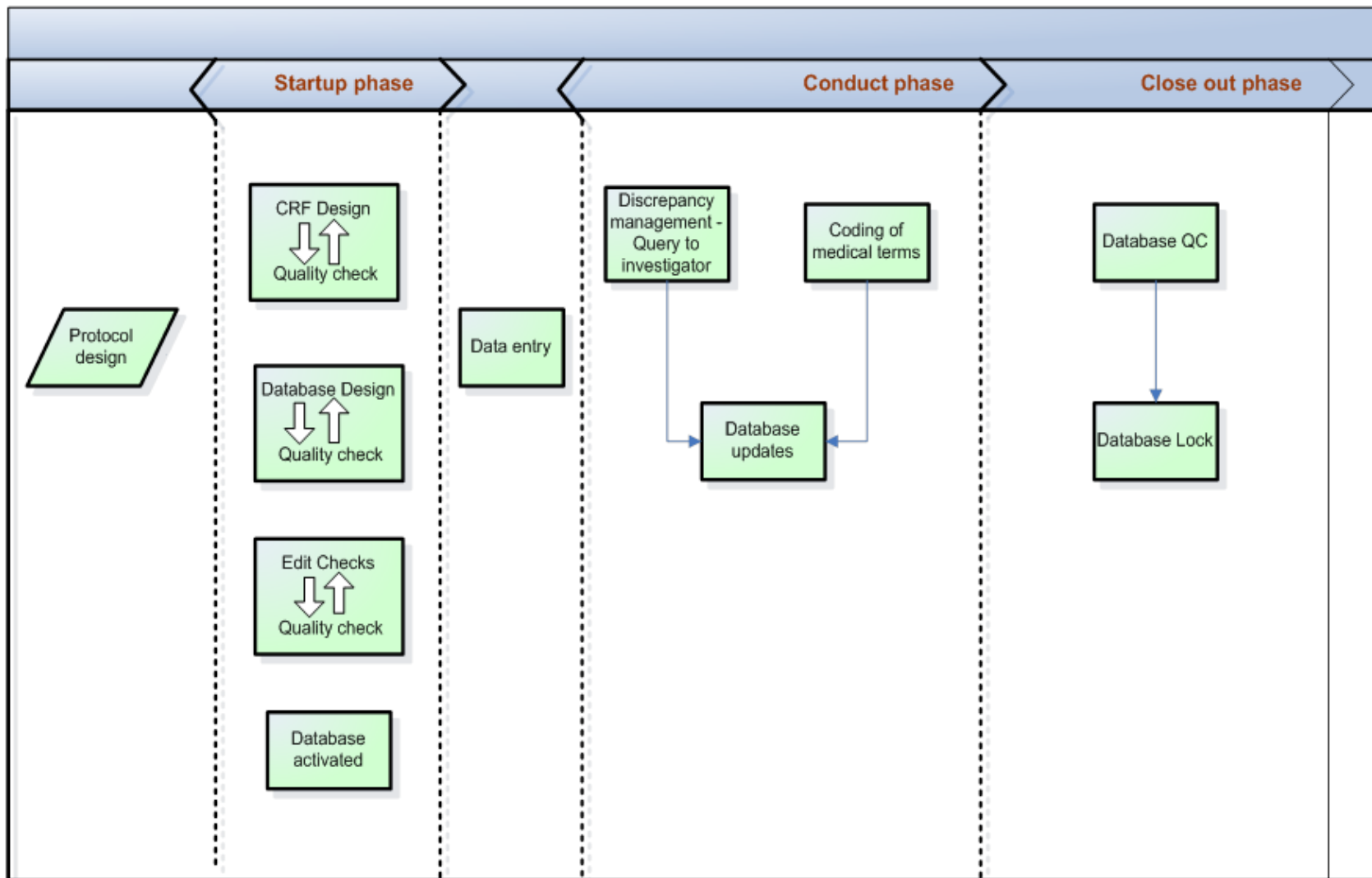
- Data Entry
- Discrepancy Management
- Data Coding (using MedDRA and WHODDE dictionaries)
- Data review (Ongoing QC)
- SAE Reconciliation
- Data Transfer

Study Closeout

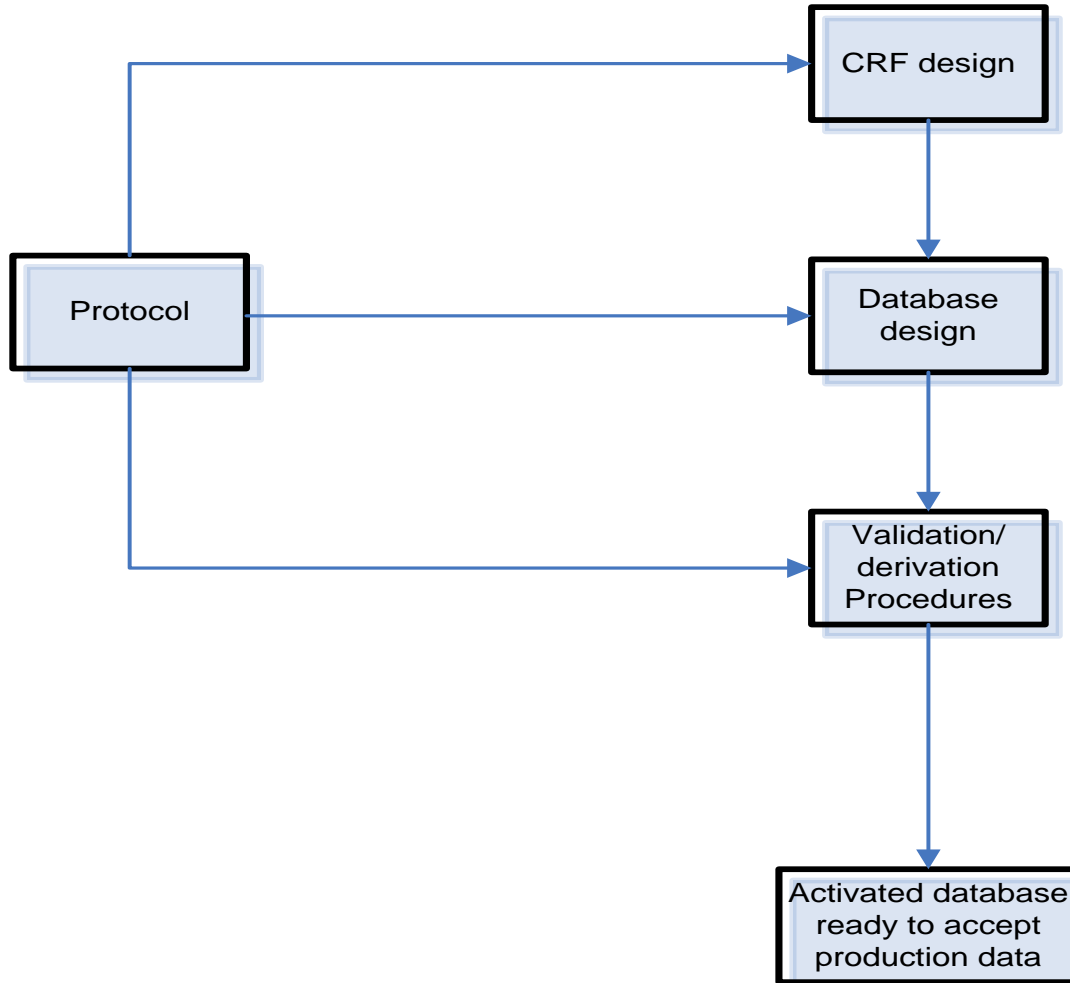
- SAE Reconciliation
- Quality Control
- Database Lock
- Electronic Archival
- Database Transfer



CDM Process Overview



Study Start Up Process Review



CRF Design/Review

A representation of the study as outlined in the protocol is made (including CRF completion guidelines if necessary). Therefore a final protocol needs to be available before this activity can be initiated. CRF design usually takes about three rounds: First draft (rough without detail but correct content), second draft (as good as we can get it) and final version. We need input from our sponsor to correct draft versions and to approve the final version.

QADATA EDC

- Traditional Paper Based Case Report Forms
- e-CRF (Electronic Case Report Form)- Study information directly entered into computer.

LYME DISEASE CASE REPORT FORM

Patient's last name _____ First name _____ Tele No. () _____
 Address _____ City _____

 Detach before sending to CDC

 State _____ County _____ Zip _____
 Age (yrs.) _____ Sex M Race Amer. Indian/Eskimo Ethnicity Hispanic
 F Asian/Pacific Isl. Non Hisp.
 Unspec. Black Unknown
 White
 Unknown

SYMPTOMS AND SIGNS OF CURRENT EPISODE (PLEASE MARK EACH QUESTION)

DERMATOLOGIC:
 Erythema migrans (physician diagnosed EM at least 5 cm in diameter)?[Y] [N] [?]
RHEUMATOLOGIC:
 Arthritis characterized by brief attacks of swelling in one or a few joints?[Y] [N] [?]
NEUROLOGIC:
 Bells palsy or other cranial neuritis? [Y] [N] [?]
 Radiculoneuropathy? [Y] [N] [?]
 Lymphocytic meningitis? [Y] [N] [?]
 Encephalitis [Y] [N] [?]
 Antibody to burgdorferi higher in CSF than serum? [Y] [N] [?] or not tested | |
CARDIOLOGIC:
 2nd or 3rd degree atrioventricular block?[Y] [N] [?]
Other clinical:

Date of onset of first symptoms: / / Date of diagnosis: / / Date of report to health agency: / /
 mo dy yr mo dy yr mo dy yr

OTHER HISTORY

Was the patient hospitalized for the current episode?[Y] [N] [?]
 Name of antibiotic(s) used this episode? _____ Use in days _____
 Was the patient pregnant at the time of the illness?[Y] [N] [?]
 Where was the patient most likely exposed? County _____ State _____

LABORATORY RESULTS

	Positive	Negative	Equivocal	Not done/Unknown
Serologic test results:	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Culture results	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Other (specify)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

The screenshot shows a web-based interface for entering case data. At the top, it displays user information: 'User: Laurie Benyair', 'ID: 551_LBN/P888', and 'Database: TESECOS/06'. A navigation pane on the left lists various site management tools like 'Subject List', 'Task List', and 'CRFs in Progress'. The main content area shows a study overview for '999-00105 (M)' with a timeline of visits from May 20, 2012, to June 20, 2012. Below this is a detailed form for 'VISIT 1' with sections for 'INFORMED CONSENT', 'DEMOGRAPHICS', and 'BCG VACCINATION'. The 'INFORMED CONSENT' section shows 'Date informed consent signed' as 18May2012. The 'DEMOGRAPHICS' section shows 'Date of Birth' as 12 JUL 1972 and 'Race' as White. The 'BCG VACCINATION' section shows 'Has the patient had a prior BCG vaccination?' as No. At the bottom right, the system clock shows '02:27 PM 2012/10/01'.

Paper CRF

e-CRF

How many CRFs do you need?

- Eligibility or Screening
- Randomisation
- Physical Exam / Vitals
- Medical History
- Follow-up Visit
- AE form/ SAE form
- Concomitant therapy form
- Laboratory test form
- Status Evaluation



Data Base Design

Data from a clinical trial will be collected and stored in the CDMS

A database is simply a structured set of data.

A collection of rows and columns.

--QAData CDMS



Subject Id	Name of patient	Age	Sex
A23691	XYZ	23	M
A23692	XYA	24	M
A23693	XYB	25	F
A23695	ABX	26	M

DBMS:

MS Access, MS Excel

Oracle Clinical

Clintrial

Phaseforward InForm

medidata Rave

CRF Annotation

- An annotated CRF is generally defined as a blank CRF with markings, or annotations, that coordinate each data point in the form with its corresponding dataset name.
- Essentially, an annotated CRF communicates where the data collected for each question is stored in the database.
- CRF Annotation is the first step in translating the CRFs into a database application.
- CDM annotates the CRFs by establishing variable names for each item to be entered.
- Reviewed by CDM and Statistician

CIV

	VISIT 1, DAY 1	Site/Subject Number: _ _ - _ _ _ _	Page 1 of 33
	Date of Visit: _ _ / _ _ / _ _ _ _	VISDAT	
	DD	MON	YYYY

DS

INFORMED CONSENT			
NO study related activities may take place before the patient has signed the Informed Consent form.			
Date informed consent was obtained:	_ _ / _ _ / _ _ _ _	DVSTDAT	
	DD	MON	YYYY
Time informed consent was obtained:	_ _ : _ _	DSSTTIM	
	24hr clock		

DM

DEMOGRAPHICS			
Date of Birth:	_ _ / _ _ / _ _ _ _	BRTHDAT	

Validation Checklist:

Edit specifications list describes in detail which data shall be checked and queried if necessary. The programming of the checks occurs according to this list. Before the programming starts, the sponsor will be asked to give approval of this list.

Test subjects are entered in the database to test the entry screens and the programming. The exact number of test subjects is not standard, but every check has to pass and fail (negative and positive proof) at least once.

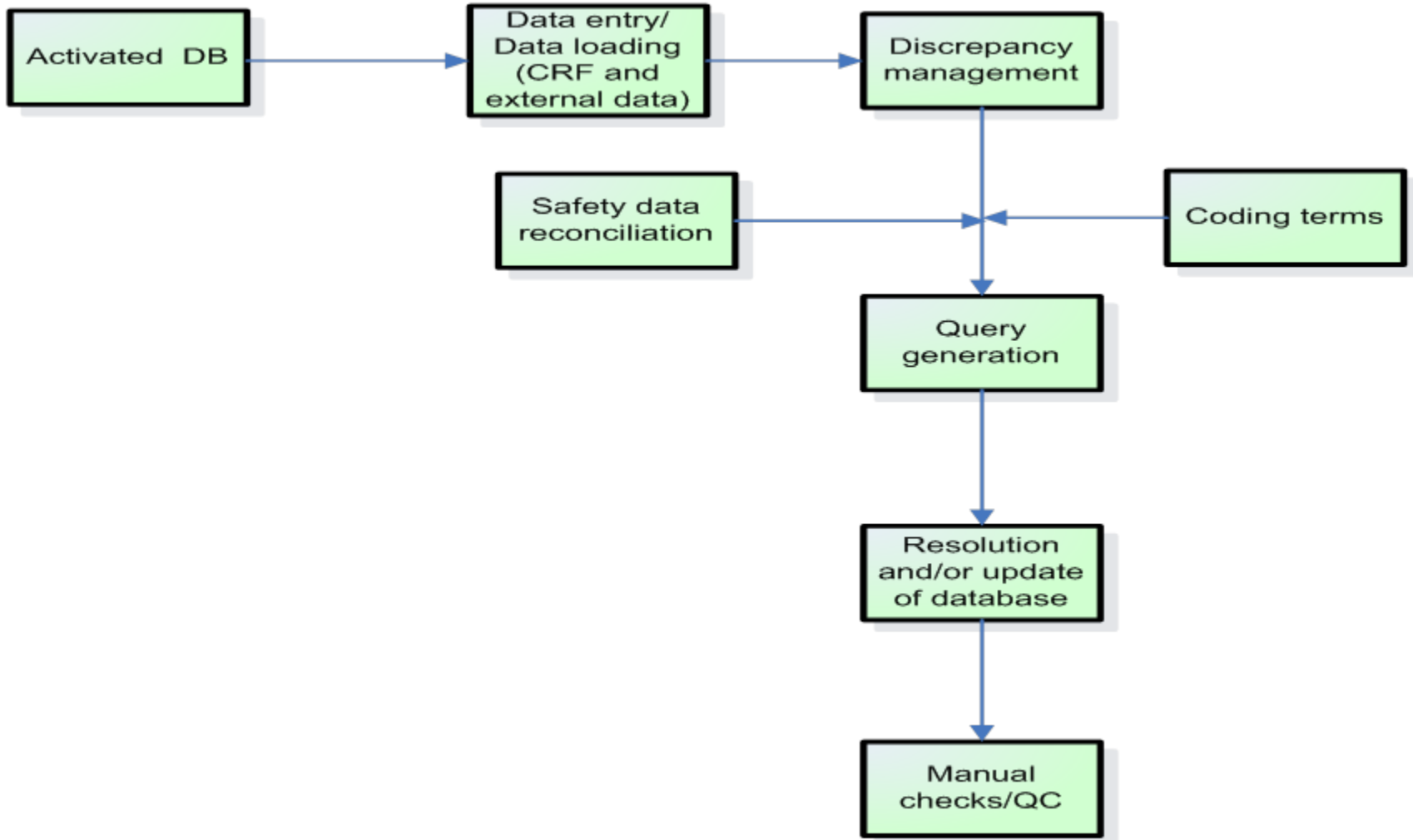
Database set up and testing

Database setup and testing are always performed in a secure, non study data environment (test site). Only when a database has been reviewed and fully tested, will it be set in 'production', a separate environment where only study data will be entered.

Changes in structure or programming will always first be performed and tested in the non study data environment before they are made effective in the 'production' database.

B	C	D	F	G	H	I	J	K
table_name	crf_section_name	column_name	CRF Page	DCF Type	Query text	Test Condition	Test Plan	Pass/Fail, Date, Patient number
EHARD_CIV	All	invdat	Vis 1 page 10/Vis 2 page 14/ Vis 3 page 18/ Vis 4 page 23/ Vis 5 page 28	Blank	Investigator date has not been completed, please provide.	Visit 1	Q: Investigator date = blank NQ: Investigator date = 10JUN2012	P, 99-010, 25SEP2012
EHARD_DS	Informed consent	dvstdat	Visit 1 Day 1	Blank	Date of informed consent has not been completed, please check and provide		Q: Consent date = blank NQ: Consent date = 01JUN2012	P, 99-010, 12SEP2012
EHARD_DS	Informed consent	dvstdat	Visit 1 Day 1	invalid	Date of informed consent may not be after Visit 1 date, please check.	Date of visit 1 = 01JUN2012	Q: Consent date = 02JUN2012 NQ: Consent date = 01JUN2012 NQ: Consent date = 31MAY2012	P, 99-010, 12SEP2012
EHARD_DS	Informed consent	dssttm	Visit 1 Day 1	Blank	Time of informed consent has not been completed, please check and provide		Q: Consent time = blank NQ: Consent time = 08:00	P, 99-010, 12SEP2012
EHARD_DS (E)	Inclusion / Exclusion criteria review	ieyn	Visit 1 Day 1 page 7	Blank	Did the subject meet all eligibility criteria is not completed, please check and provide details		Q: Subject met all eligibility criteria = Blank NQ: Subject met all eligibility criteria = Yes	P, 99-010, 12SEP2012
EHARD_DS	Inclusion / Exclusion criteria review	ieincl	Visit 1 Day 1 page 7	Blank	Is the subject eligible to continue is not completed, please check and provide details		Q: Patient included in the study = blank NQ: Patient included in the study = Yes	P, 99-010, 21SEP2012
EHARD_DS	Inclusion / Exclusion criteria review	ietestcd	Visit 1 Day 1 page 7	invalid	Reason has not been specified, but 'No' answered above, please check	Patient included in the study = No	Q: Reason = blank NQ: Reason = ABC	P, 99-010, 21SEP2012
EHARD_DS	Inclusion / Exclusion criteria review	ietestcd	Visit 1 Day 1 page 7	Questionable	Reason has been specified, but 'Yes' answered above, please check	Reason for non-inclusion = ABC	Q: Patient included in the study = Yes NQ: Patient included in the study = No NQ: Patient included in the study = Yes	F, 99-010, 21SEP2012

Study Conduct Process Review





CRF Tracking

Logistic way if it is paper based study.
EDC-electronic data capture if it is e-CRF.
Data Entry

Data Entry

Data entry is a process of entering/transferring data from case report form to the Clinical Data Management System (CDMS).

Data Entry: 1) Single data Entry
2) Double Data Entry



Discrepancy Management

Discrepancy management is a process of cleaning subject data in the Clinical Data Management System (CDMS), it includes manual checks and programmed checks. Trivial discrepancies are closed as per self evident correction method or Internal rulings and discrepancies which require response from the site are queried by raising Data Clarification Forms (DCF).



Medical Coding

The medical coding for a study is done as per the project specific protocol requirement. The dictionaries used for a study are:

Adverse Events: MedDRA (Medical Dictionary for Regulatory Activities)

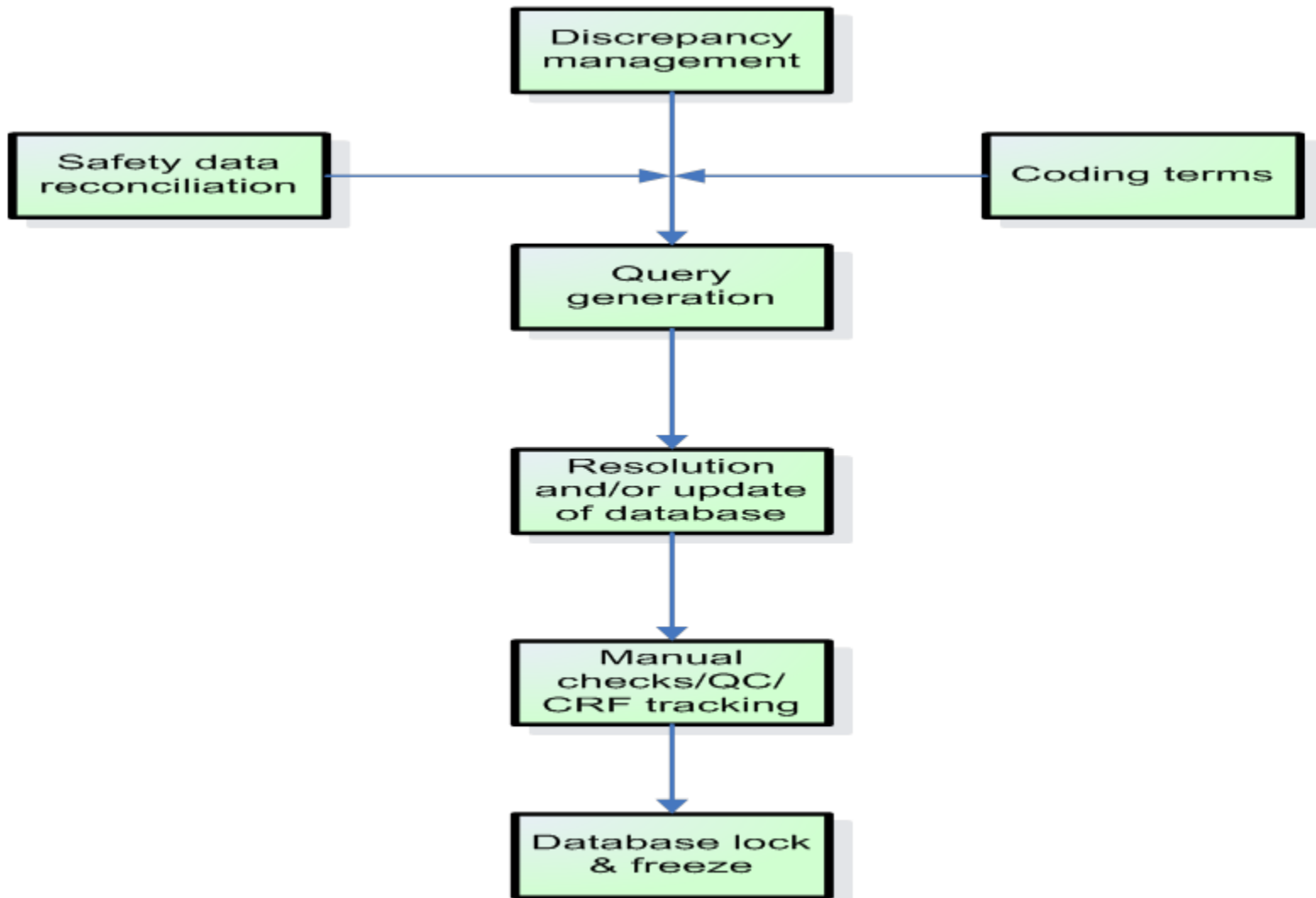
Medications: WHODD (World Health Organization – Drug Dictionary)



SAE Reconciliation

- Serious Adverse Event (SAE) data reconciliation is the comparison of key safety data variables between Clinical Data Management System (CDMS) and Sponsor PV. Reconciliation is performed to ensure that events residing in both systems are consistent.

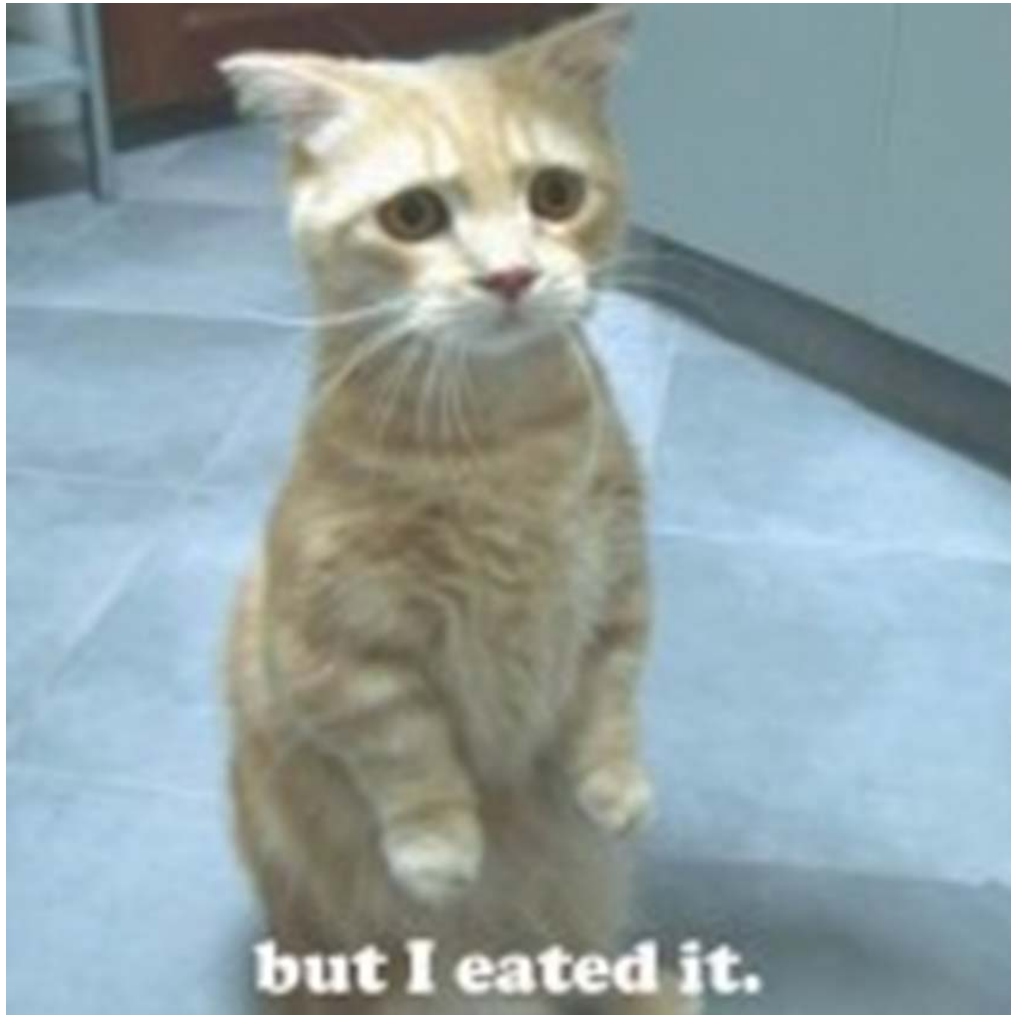
Study Close out Process Review



Quality Control

- Quality Should be maintained for overall study by performing Quality checks at intervals for all data points (Critical & Non-Critical) prior to database lock.
- QC helps to ensure that all the data processed is accurate, clean and Correct.





but I ate it.

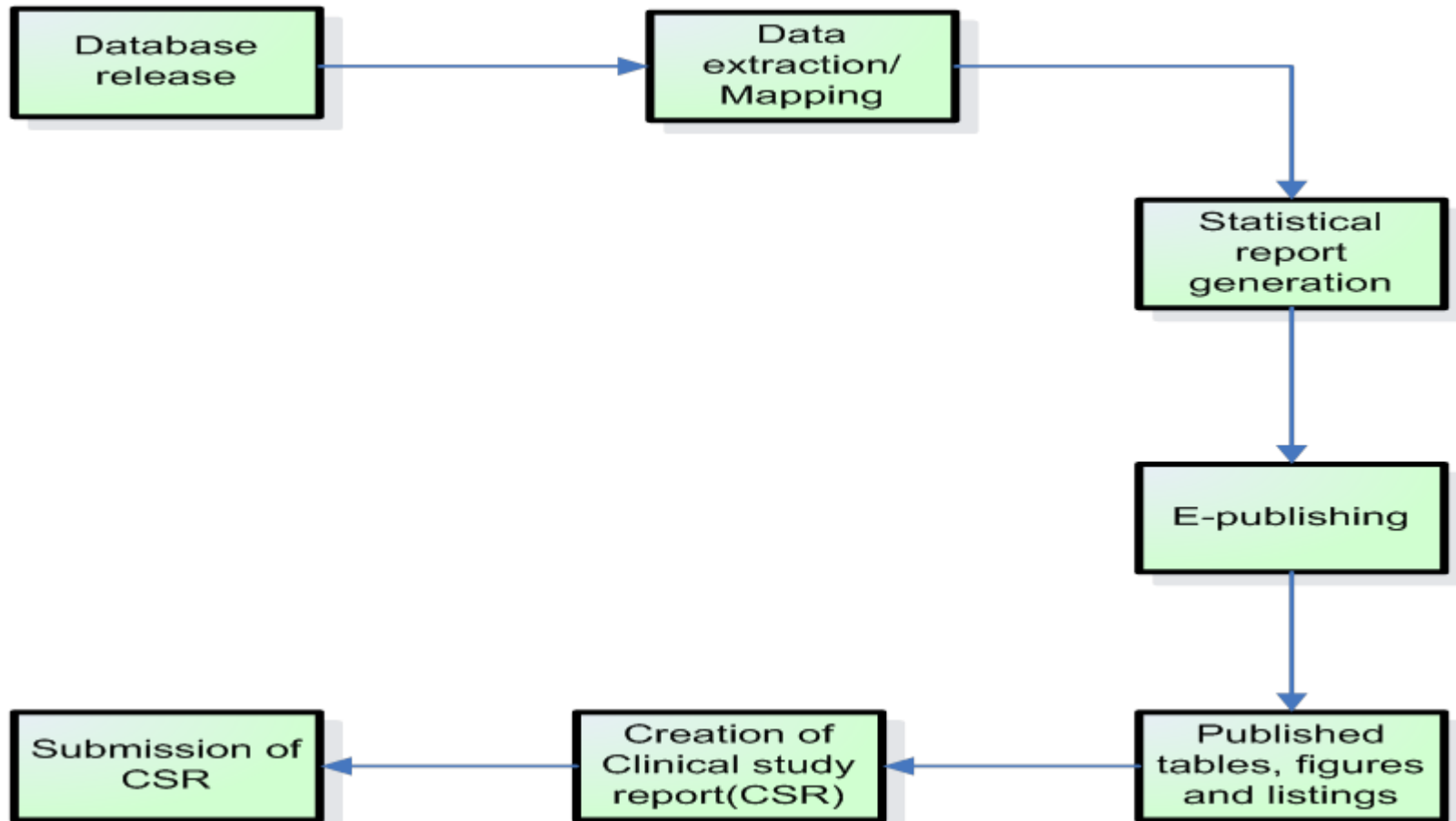
Database Lock

The database lock for a study is done to ensure no manipulation of study data during the final analysis.

Database lock for a study is done once all data management activities are completed. This includes the database lock checklist which ensures the same. Some of the activities included in database lock checklist are All discrepancies closed, DCFs received and updated, coding complete, SAE Reconciliation process complete etc.



Analysis & Reporting Process Review



Objectives of CMD

- CDM is a vital vehicle in Clinical Trials to ensure:
- The Integrity & quality of data being transferred from trial subjects to a database system
- That the collected data is complete and accurate so that results are correct
- That trial database is complete and accurate, and a true representation of what took place in trial
- That trial database is sufficiently clean to support statistical analysis, and its subsequent presentation and interpretation

Importance of CMD

CDM has evolved from a mere data entry process to a much diverse process today

- It provides data and database in a **usable** format in a **timely** manner
- It ensures **clean** data and a '**ready to lock**' database

CDM Professionals

- ICH.E6.5.5.1: Utilize qualified individuals to:
- Supervise overall conduct of trial (Project Manager)
- To handle and verify the data (Data Manager)
- To conduct the statistical analysis (Biostatistician)
- To prepare study reports (Medical Writer)

DM Role in Clinical Research

The data management function provides all data collection and data validation for a clinical trial program

Data management is essential to the overall clinical research function, as its key deliverable is the data to support the submission

Assuring the overall accuracy and integrity of the clinical trial data is the core business of the data management function

DM Role in Clinical Research

Data management starts with the creation of the study protocol

At the study level, data management ends when the database is locked and the Clinical Study Report is final

At the compound level (of the drug), data management ends when the submission package is assembled and complete

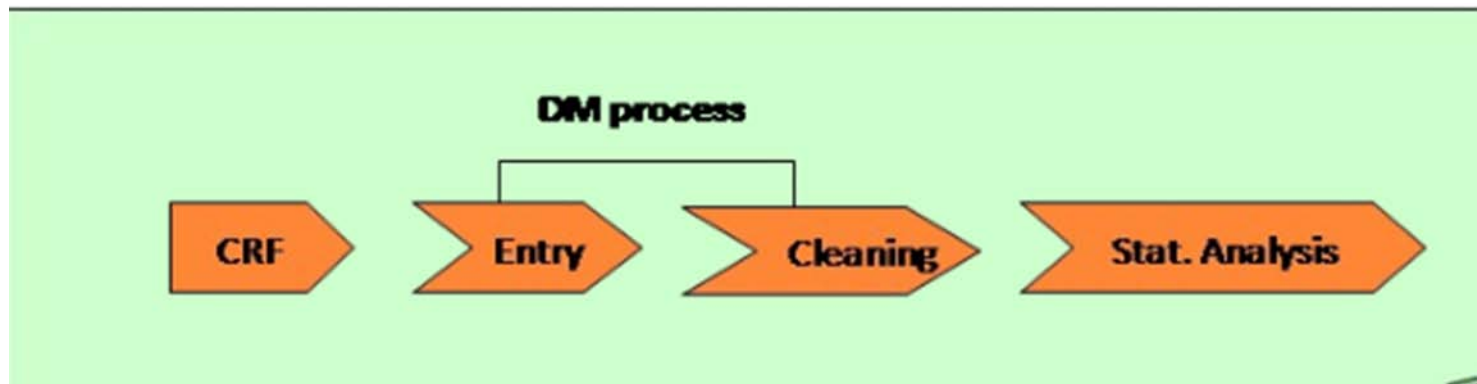
Mission of CDM

Consistency

Accuracy

Validity

Archiving



DATA MANAGEMENT WORKFLOW

