

Accelerated Approval

When studying a new drug, it can sometimes take many years to learn whether a drug actually provides a real effect on how a patient survives, feels, or functions. A positive therapeutic effect that is clinically meaningful in the context of a given disease is known as “clinical benefit”.

Mindful of the fact that it may take an extended period of time to measure a drug’s intended clinical benefit, in 1992 FDA instituted the *Accelerated Approval* regulations. These regulations allowed drugs for serious conditions that filled an unmet medical need to be approved based on a surrogate endpoint. Using a surrogate endpoint enabled the FDA to approve these drugs faster.

In 2012, Congress passed the Food and Drug Administration Safety Innovations Act (FDASIA). Section 901 of FDASIA amends the Federal Food, Drug, and Cosmetic Act (FD&C Act) to allow the FDA to base accelerated approval for drugs for serious conditions that fill an unmet medical need on whether the drug has an effect on a surrogate or an intermediate clinical endpoint.

A surrogate endpoint used for accelerated approval is a marker - a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Likewise, an intermediate clinical endpoint is a measure of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on irreversible morbidity and mortality (IMM).

The FDA bases its decision on whether to accept the proposed surrogate or intermediate clinical endpoint on the scientific support for that endpoint. Studies that demonstrate a drug’s effect on a surrogate or intermediate clinical endpoint must be “adequate and well controlled” as required by the FD&C Act.

Using surrogate or intermediate clinical endpoints can save valuable time in the drug approval process. For example, instead of having to wait to learn if a drug actually extends survival for cancer patients, the FDA may approve a drug based on evidence that the drug shrinks tumors, because tumor shrinkage is considered *reasonably likely to predict* a real clinical benefit. In this example, an approval based upon tumor shrinkage can occur far sooner than waiting to learn whether patients actually lived longer. The drug company will still need to conduct studies to confirm that tumor shrinkage actually predicts that patients will live longer.

Where confirmatory trials verify clinical benefit, FDA will generally terminate the requirement. Approval of a drug may be withdrawn or the labeled indication of the drug changed if trials fail to verify clinical benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the drug (e.g., show a significantly smaller magnitude or duration of benefit than was anticipated based on the observed effect on the surrogate).

Fast Track

Fast track is a process designed to facilitate the development, and expedite the review of drugs to treat serious conditions and fill an unmet medical need. The purpose is to get important new drugs to the patient earlier. Fast Track addresses a broad range of serious conditions.

Determining whether a condition is serious is a matter of judgment, but generally is based on whether the drug will have an impact on such factors as survival, day-to-day functioning, or the likelihood that the condition, if left untreated, will progress from a less severe condition to a more serious one. AIDS, Alzheimer's, heart failure and cancer are obvious examples of serious conditions. However, diseases such as epilepsy, depression and diabetes are also considered to be serious conditions.

Filling an unmet medical need is defined as providing a therapy where none exists or providing a therapy which may be potentially better than available therapy.

Any drug being developed to treat or prevent a condition with no current therapy obviously is directed at an unmet need. If there are available therapies, a fast track drug must show some advantage over available therapy, such as:

- Showing superior effectiveness, effect on serious outcomes or improved effect on serious outcomes
- Avoiding serious side effects of an available therapy
- Improving the diagnosis of a serious condition where early diagnosis results in an improved outcome
- Decreasing a clinically significant toxicity of an available therapy that is common and causes discontinuation of treatment
- Ability to address emerging or anticipated public health need

A drug that receives *Fast Track* designation is eligible for some or all of the following:

- More frequent meetings with FDA to discuss the drug's development plan and ensure collection of appropriate data needed to support drug approval
- More frequent written communication from FDA about such things as the design of the proposed clinical trials and use of biomarkers
- Eligibility for *Accelerated Approval* and *Priority Review*, if relevant criteria are met

<https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/fast-track>

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Fast Track | FDA

- *Rolling Review*, which means that a drug company can submit completed sections of its Biologic License Application (BLA) or New Drug Application (NDA) for review by FDA, rather than waiting until every section of the NDA is completed before the entire application can be reviewed. BLA or NDA review usually does not begin until the drug company has submitted the entire application to the FDA

Fast Track designation must be requested by the drug company. The request can be initiated at any time during the drug development process. FDA will review the request and make a decision within sixty days based on whether the drug fills an unmet medical need in a serious condition.

Once a drug receives *Fast Track* designation, early and frequent communication between the FDA and a drug company is encouraged throughout the entire drug development and review process. The frequency of communication assures that questions and issues are resolved quickly, often leading to earlier drug approval and access by patients.

Priority Review

Prior to approval, each drug marketed in the United States must go through a detailed FDA review process. In 1992, under the Prescription Drug User Act (PDUFA), FDA agreed to specific goals for improving the drug review time and created a two-tiered system of review times – *Standard Review* and *Priority Review*. A Priority Review designation means FDA's goal is to take action on an application within 6 months (compared to 10 months under standard review).

A *Priority Review* designation will direct overall attention and resources to the evaluation of applications for drugs that, if approved, would be significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications.

Significant improvement may be demonstrated by the following examples:

- evidence of increased effectiveness in treatment, prevention, or diagnosis of condition;
- elimination or substantial reduction of a treatment-limiting drug reaction;
- documented enhancement of patient compliance that is expected to lead to an improvement in serious outcomes; or
- evidence of safety and effectiveness in a new subpopulation.

FDA decides on the review designation for every application. However, an applicant may expressly request priority review as described in the Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics. It does not affect the length of the clinical trial period. FDA informs the applicant of a Priority Review designation within 60 days of the receipt of the original BLA, NDA, or efficacy supplement. Designation of a drug as "Priority" does not alter the scientific/medical standard for approval or the quality of evidence necessary.

16. SAFETY MONITORING IN CLINICAL TRIALS

INTRODUCTION:

1. Clinical trials are a cornerstone in medical advances; hence there is a progress in the design and conduct of a clinical trial.
2. This lead to an increased awareness of ethical issues and safety monitoring.
3. Hence a system should be there to ensure the safety of participants.
4. The establishment of a **Data safety monitoring boards (DSMB)** is required for clinical trials, involving potential risks to the patients.

According to the principles of ICH-GCP guidelines:

- The rights, safety and well being of the trial subjects are the most important considerations.
- Safety Monitoring is done by:
 1. Investigator
 2. IRB/IEC`s
 3. Sponsor
 4. Monitor

1. Investigator - responsibility:

During and following subject participation in a trial, the investigator should ensure that the adequate medical care is provided to the subjects for any adverse events, related to the trial [ICH-GCP 4.3.2]

2. IRB/IEC - responsibility:

- An IRB/IEC should safeguard the rights, safety and well being of all trial subjects.[ICH-GCP 3.1.1]
- The IRB IEC should conduct continuing review of each ongoing trial, at definite intervals. At least once per year.

3. Sponsor - responsibility:

Sponsor may consider establishing an independent data monitoring committee (IDMC) (or) DSMB to assess the progress of a clinical trial, which includes the safety data and to recommend to the sponsor, whether to continue, modify or stop a trial [ICH-GCP 5.5.2]

4. Monitor - responsibility:

Determining whether all adverse events are properly reported within the time period required by:

1. GCP
2. Protocol
3. IRB/IEC
4. Sponsor and
5. Applicable regulatory requirements. [ICH-GCP-5.18.4]

SAFETY MONITORING IN DIFFERENT PHASES OF CLINICAL TRIALS

Phase-I:

Experimental drug given in a small group of people (20-80) to evaluate its **safety, determine a safe dosing range, identify side effects.**

Phase-II:

Experimental (study) drug is given to a large group of people (100-300) to see **its effectiveness and to further evaluate safety.**

Phase-III:

Experimental drug is given to a large group of people (1000-3000) to confirm its effectiveness, monitor side effects, and collect information for safety.

Phase-IV:

- 1. Post marketing studies, gives additional information includes drug risks, benefits, and optimal use.**
- 2. For drugs being studied under investigational new drug application [INDA], the FDA published a regulation, establishing a new safety reporting paradigm.**
- 3. According to this clinical investigator and sponsor have to be more responsible in reporting and analysis of serious, unexpected events that might be caused by drug.**

Types of Monitoring



1) Central monitoring.

- Determination of key eligibility criteria through collection of:
 - Consent forms
 - Scans
 - Pathology reports
- Statistics
 - Unusual patterns of data.



ICH GCP 5.18.3

Types of Monitoring



2) Risk Based monitoring.

ICH GCP 5.18.3

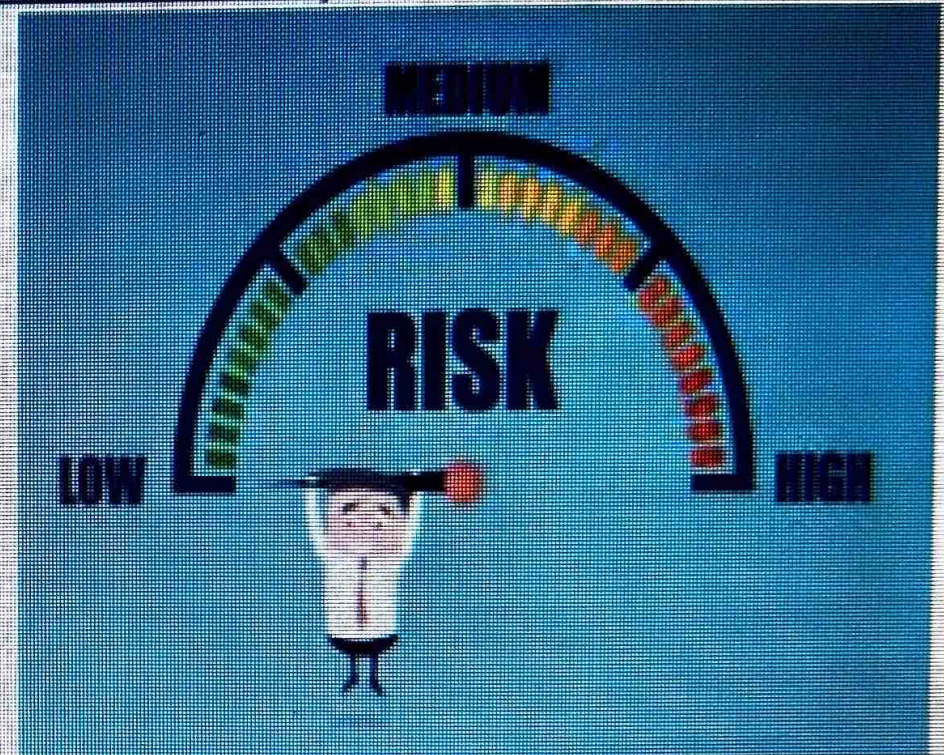
☐ Limited resources should be used to where it is really necessary.

High risk part.

- For subject protection
- For reliability of trial results
- For protection of future patients

☐ Risk-based approach! (6 Rs)

- 1- Risk Identification
- 2- Risk Evaluation
- 3- Risk Control
- 4- Risk Communication
- 5- Risk Review
- 6- Risk Reporting



ICH GCP Sections 2.13, 5.0 (, 5.20.1)

Types of Monitoring Cont..



3) On site Monitoring.

- Staff training
- Access to necessary documents
- Confirm pharmacy and lab resources in place
 - * Count study drug
- Adherence to protocol and GCP
- Check medical records
 - * Consent forms
 - * Eligibility
 - * AEs
- Source Data Verification (SDV)

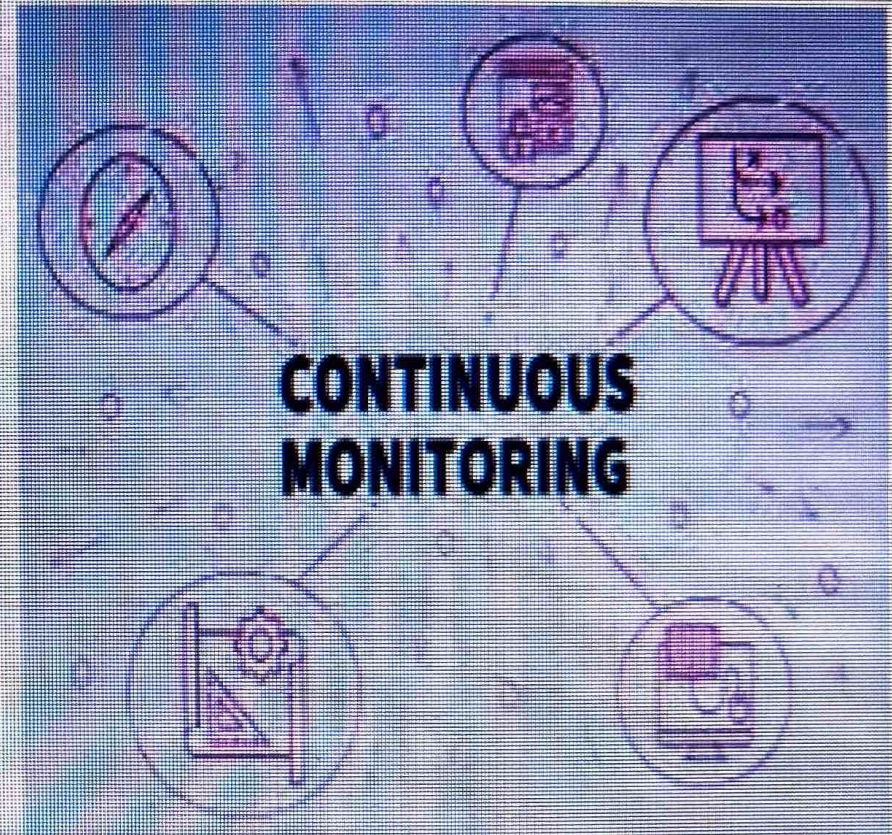


Monitoring Process Continued..



1) Before Monitoring Visit :

- Review the status of data entry
- Review action item from last visit
- Review regulatory binder
- Check PI & site staff availability
- Get the internal team approval
- Send confirmation/agenda of monitoring visit



Monitoring Process Continued..



2) During Monitoring Visit.

- The monitor will assess or discuss:

- ❖ Site, staffing, research labs or other facilities
- ❖ Regulatory file and study records
- ❖ Clinical procedures if possible or appropriate
- ❖ Any problems and issues identified
- ❖ Debrief at end of visit

Monitoring Process Continued..



3) After Monitoring Visit.

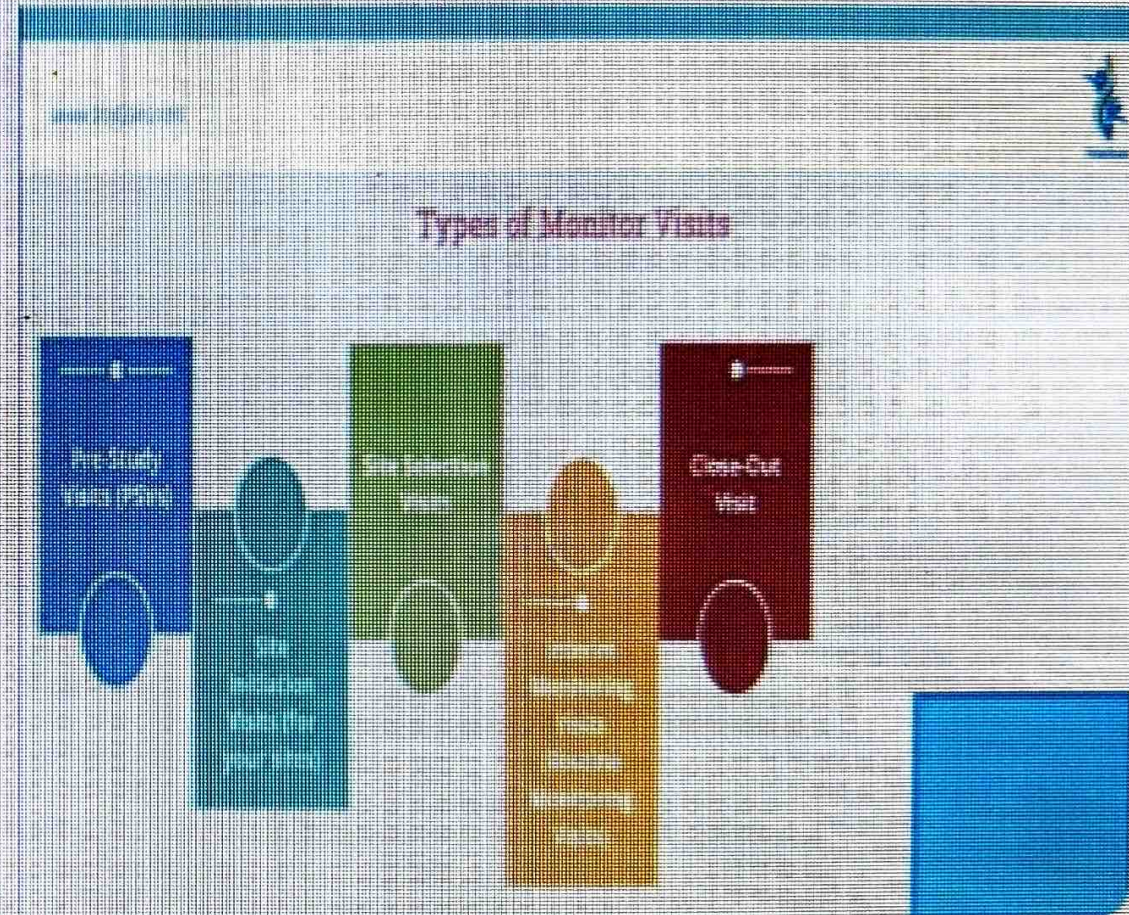
The monitor will.....

- ❖ Complete site visit report
- ❖ Submit the report to the sponsor

4 Types Monitoring Visits



- 1) Site assessment(pre trial) Visit
- 2) Site initiation Visit
- 3) Routine(interim) visit
- 4) Close Out Visit

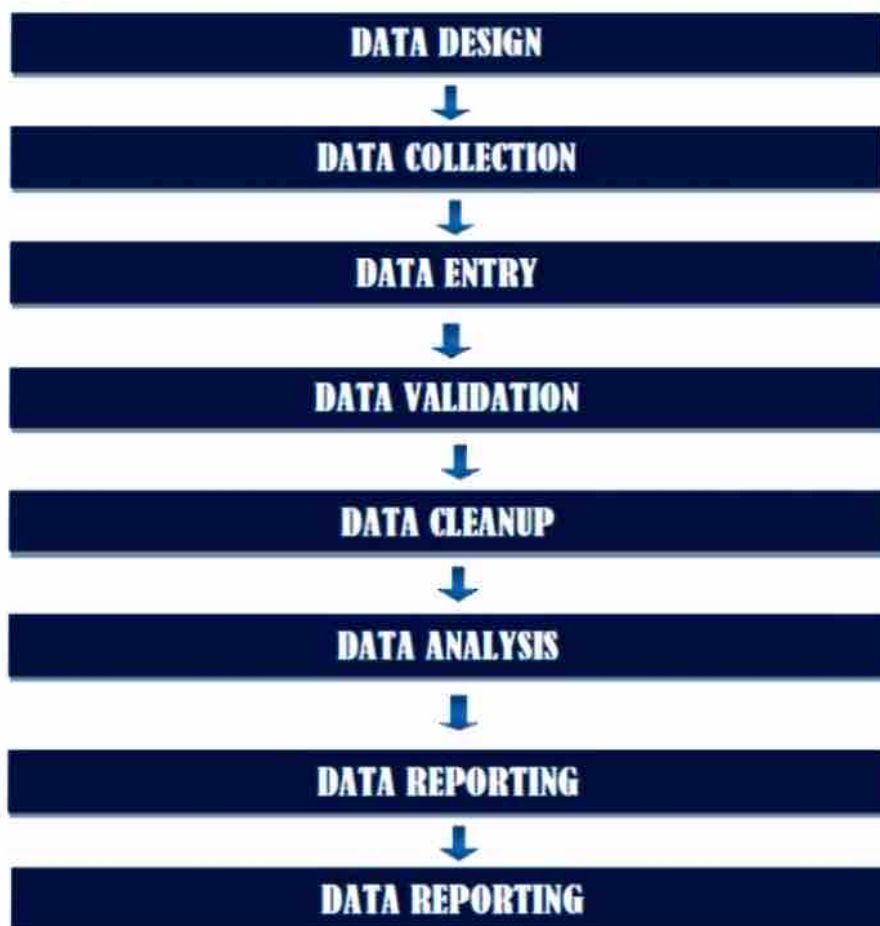


15. DATA MANAGEMENT & ITS COMPONENTS

- Clinical data management is the collection, integration, and validation of clinical trial data.
- During the clinical trial, the investigators collect the data of patient's health for a definite time period.
- The collected data is sent to the sponsor, who then analyzes the pooled data using statistical analysis.
- This data gathered at the investigator site in the Case Report Form (CRF) and stored in Clinical data management system.
- CRF is a paper or electronic questionnaire, used as a tool in the clinical trial to collect and record the data on each patient from each participating site.

CRFs allow us to:

- Record the data in a manner that is both efficient and accurate.
- Recording the data in a manner is suitable for processing, analysis, and reporting.



STEPS IN DATA MANAGEMENT PROCESS

Sequential steps in Data Management:

➤ Data Design:

- The database allows for adequate storage of study data and for accurate reporting, interpretation, and verification of the data. Two database systems tend to co-exist alongside one another.
- Study management database: personal information, recruitment, data completeness (CRF receipts) follow-up trigger.
- Clinical database: clinical information (study outcomes).

▪ Functionalities to consider in both types of database:

- Validation rules (Ranges, skips, Inconsistencies.)
- Queries / report.
- Audit trail.

➤ Data Collection:

- The validity of data collection must be ensured.
- Source data is identified and transcribed correctly into a data collection system.
- Process of data collection/transcription is audited throughout the process (monitoring - Source data verification).

▪ Before starting data collection:

• Testing:

1. After set-up, test or pilot the system before you use it.
2. Maintain an adequate record of this procedure.

• SOP and PRA:

1. Good idea to write a Standard Operating Procedure or a working practice document detailing how you set up your electronic data capture systems.
2. The appropriate persons need to be trained in these.

3. Need to write a Privacy Risk Assessment, this document includes:

- A. Personal data items held in study E.g. Name, DOB.
- B. Individuals who are granted access to this data.
- C. Procedures for collecting, storing, and sharing personal data.
- D. How personal data will be anonymized.
- E. Identifying possible breaches of confidentiality and how these can be reduced.

- **Training:**

1. After piloting, when it is working as it should, the next step is to train all users.
2. A record should be maintained at the training.
3. A detailed diagram and description of how data will be collected should be provided at the training.

- **During data collection:**

- **Audit:**

1. Maintain an audit trail of data changes made in the system.
2. Procedure to correct the data, when the operator has made a mistake.
3. Important that original entries are visible or accessible to ensure the changes are traceable.

- **Safe Collection of Data:**

- The safe collection of data in clinical trials is essential for compliance with Good Clinical Practice and the Data Protection Act 1998.
- Because of increased use of information technology in the collection of trial data clear guidance is needed on how to safely collect the data in a manner.
- Need to protect your data from loss or unauthorized access, at the same time ensuring that it is accessible to those who need it.

➤ **Data Entry:**

- Different types of data entry have existed (manual /optical mark recognition system, online/offline, etc.).
- Type of data can also influence the method of data entry (numerical, free text, images, etc).
- It is important to have documented procedures (SOPs) defining who is performing data entry and how it is performed.
- Data entry procedures should be tested at the earlier design stage and testing adequately documented before sign-off.
- Adequate training on these procedures should be provided.
- Appropriate quality control procedures have to be set up.

• **Electronic data entry:**

- Electronic data entry does not usually have to be a separate 'data entry phase', normally entered into an electronic CRF.
- Data can be entered straight onto a website or can be entered into a laptop and uploaded using the internet by the server.
- While designing the forms to collect data electronically you can include validation rules. An electronic system can stop the Researcher from proceeding with data collection if they break a validation rule.

➤ **Data Validation:**

• **Check:**

1. Ranges, skips, inconsistencies and missing data i.e. what is on your metadata is exactly, what is applied when entering the data on the form.
- Check output file for data export (for the clinical database):
 1. Variable names match up.
 2. Coding of categories correctly.
 3. Numbers when alpha required.
 4. What is on the form is transferred exactly into CSV / SPSS.

➤ **Data clean up:**

- Errors/inconsistencies/ missing data spotted at different time depending on the study and methods used.
- Errors should be corrected where possible, but no changes should be made without proper justification.
- Appropriate audit trails should be kept to document changes in the data (queries form, SPSS syntax).

➤ **Data Analysis:**

- In the majority of trials, sponsors will require appropriately trained statistician for Statistical data analysis
- One of the main components of the analysis is the statistical analysis plan (SAP). This plan ensures that the analyses to evaluate all planned study hypotheses are conducted in a scientifically valid manner and that all decisions are documented. It also provides detail on how the results will be presented and reported.
- The following should be described and agreed in the SAP:
 1. Any primary and key secondary outcome measures stated in the protocol to be analyzed.
 2. Methods for handling missing data and multiplicity of data.
 3. Justification for any non-standard statistical techniques.
- **Some Statistical Approaches to Analysis of Clinical Trials:**
 - Hierarchical models
 - Bayesian analysis
 - Decision analysis
 - Sequential analysis
 - Statistical prediction
 - Meta-analysis and other alternatives
 - Risk-based allocation

➤ **Data Reporting:**

- Throughout the course of the study, it is the responsibility of the Data Manager to report the study progress, this kind of reports includes:
 1. Recruitment progress
 2. Follow-up rates
 3. SAE Reconciliation
 4. Data completeness
 5. Withdrawals

➤ **Database Lock:**

- The database lock for a study is done to ensure no manipulation of study data during the final analysis.
- This is done once all data management activities are completed. This includes the database lock checklist which ensures the same. Some of the activities included a database lock list checklist are all discrepancies closed, data collection forms received and updated, coding complete and SAE reconciliation process, etc.

➤ **Data Presentation:**

- Data presentation can be done in graphical methods by some of the statistical approaches.

Objectives:

- The integrity and quality of data being transferred from trial subjects to a database system.
- It ensures the collected data is accurate and complete so that the results are correct.
- The trial database is accurate and complete so true representation takes place in the trial.
- The trial database is sufficient to clean statistical analysis and its subsequent presentation and interpretation.

7.3.1. **Definitions:**

Medical devices: A medical device is defined as an inert diagnostic or therapeutic article that does not achieve any of its principal intended purposes through chemical action, within or on the body unlike the medicated devices which contain pharmacologically active substances which are treated as drugs. Such devices include diagnostic test kits, crutches, electrodes, pacemakers, arterial grafts, intra-ocular lenses, orthopaedic pins and other orthopaedic accessories.

Depending upon risks involved the devices could be classified as follows:

- a. **Non critical devices:** An investigational device that does not present significant risk to the patients. e.g. Thermometer, B.P. apparatus.
- b. **Critical devices:** An investigational device that presents a potential risk to the health, safety, welfare of the subject- for example, pacemakers, implants, internal catheters.

All the general principles of clinical trials described for clinical trials should also be considered for trials of medical devices. As for the drugs, safety evaluation and pre-market efficacy of devices for 1-3 years with data on adverse reactions should be obtained before pre-market certification. The duration of the trial and extent of use may be decided in case to case basis by the appropriate authorities. However, the following important factors that are unique to medical devices should be taken into consideration while evaluating the related research projects.

7.3.2. Guidelines

- o Safety data of the medical device in animals should be obtained and likely risks posed by the device should be considered.
- o 'A clinical trial of medical devices is different from drug trials, as former can not be done in healthy volunteers. Hence phase I of drug trial is not necessary for trial on devices.
- o Medical devices used within the body may have greater risk potential than those used on or outside the body, for example, orthopaedic pins Vs crutches.
- o Medical device not used regularly have less risk potential than those used regularly, for example, contact lens Vs intraocular lenses.
- o Safety procedures to introduce a medical device in the patient should also be followed as the procedure itself may cause harm to the patient.
- o Informed consent procedures should be followed as in drug trials. The patient information sheet should contain information on following procedures to be adopted if the patient decides to withdraw from the trial.

Write the guideline of ~~CDSCO~~ CDSCO.

CDSCO → central Drugs standard control organization.

Indication → To safeguard and enhance the public health by assuring the safety, efficacy and quality of drugs, cosmetics and medical devices.

Function → Directive general health services. (DGHI) → (DGHS)

- ✓ 1) Approval of new drugs and clinical trials.
- ✓ 2) Import Registration and licensing.
- ✓ 3) License approving of blood banks, vaccines, - n DNA, products and some medical devices (CLAA scheme)
- ✓ 4) Amendment to D and C Act and rules.
- ✓ 5) Banning of drugs and cosmetics.
- ✓ 6) Grant of test license, personal license, NoCs for export.
- ✓ 7) Testing of new drugs
- ✓ 8) Oversight and market surveillance through inspectorate of centre over and above the state authority.

CDSCO Steps →

DCC
DTAB

Application for permission →

Form	items	appendix.
pharmaceutical and chemical info	2	1
Animal pharmacology data	3	1, 4
Human clinical pharmacology	5, 6, 7	1
Regulatory status in other country	9, 2	1
Animal toxicology data.	4	1, 3
Full prescribing info	10	1

Clinical trials →

a) Approval clinical trial →

↳ Clinical trial on a new drug shall be initiated only after the under permission has been granted by the licensing authority under rule 21(b) and the approval obtained from the respective ethics committee.

b) Responsibilities of sponsor →

The clinical trial sponsor is responsible for implementing and maintaining quality assurance systems to ensure that the clinical trial is conducted and data generated, documented and reported in compliance with the protocol and Good clinical practice GCP guidelines.

c) Responsibilities of investigator →

The Investigator shall be responsible for the conduct of the trial according to the protocol and GCP guidelines.

d) Informed consent →

In all trials, a freely given, informed, written consent is required to be obtained from each study subject. The investigator must provide information about the study verbally as well as using a patient information sheet in a language that is non-technical and understandable by the study subject.

e) Responsibilities of the ethics committee →

It is the responsibility of the ethics committee that reviews and accords its approval to a trial protocol to safeguard the rights safety and well being of all trial subject.

f) Human pharmacology (phase I) →

The objective of studies in this phase is the estimation of safety and tolerability with the initial administration of an investigational new drug into human. Studies in this phase of development usually have non therapeutic objectives and may be conducted in healthy volunteers on certain types of patients.

g) Therapeutics exploratory trials (phase II)

The primary objective of phase II trials is to evaluate the effectiveness of a drug for a particular indication or indications in patients with the condition under study and to determine the common short-term side effects and risks associated with the drug.

h) Therapeutics confirmatory trials (phase III)

Phase III studies have primary objective of demonstration or confirmation of therapeutic benefit. Studies in phase III are designed to confirm the preliminary evidence accumulated in phase II that a drug is safe and effective for use in the intended indication and recipient population.

i) Post marketing trials (phase IV)

- ① Post marketing trials are studies performed after drug approval and related to the approved indication.
- ② These trials may not be considered necessary at the time of new drug approval but may be required by the licensing authority for optimizing the drugs' use.

III Study in special population →

- ① Pediatrics.
- ② Geriatric
- ③ Pregnant or lactating women.
- ④ People with specific disease.

Drug master file →

Are submission to FDA used to provide confidential, detailed information about facilities process or articles used in the manufacturing, processing, packing and storing of human drug products.

6) List members of ICH.

- ⇒
- ① Observers from WHO.
 - ① European Commission
 - ① Technical staff.
 - ① Scientific staff.

2) Note on CIOMS.

⇒ CIOMS → council for international organizations of medical sciences.

It represents a substantial proportion of the biomedical scientific community through its biomedical scientific community through its member organizations, which include many of the biomedical disciplines.

1) Functions of Drug Control General of India (DCGI)

- ⇒
- ① permission to conduct clinical trials with new drugs.
 - ① Import license / test license for clinical trial drug supplies. concurrent with main submission.
 - ① Approval for conducting clinical trials with medical devices under drug category.
 - ① Notification for SAEs observed in ongoing clinical trials.

6) Note on 21 CFR part 312.

⇒ This part contains procedures and requirements governing the use of investigational new drugs, including procedures and requirements for the submission to and review by the Food and Drug Administration of investigational new drug applications.

5) Define ethics.

⇒ Well-founded standards of right and wrong that prescribe what humans ought to do, usually in terms of rights, obligations, benefits to society, fairness or specific virtues.

4) List the guidelines and acts that govern the conduct of clinical trials in India.

⇒ ① Every trial has a head person in charge. Usually a doctor, who is called the principal investigator.

① The principle investigator prepares a plan for the study, called a protocol which acts like a 'recipe' for conducting a clinical trial.

② Every doctor or research center that takes part in the trial uses the same protocol.

Pregnant women are routinely excluded from phase I and II clinical drug development trials. There is a hesitation from clinicians and researchers on enrolling pregnant women in studies due to ethical concerns and possible harm to the developing fetus. Possible litigation discourages pharmaceutical industries to involve them; their inclusion requires long-term follow-up to assess fetal and newborn outcomes; and the revenue benefit is relatively small in relation to the investment. Additionally, the presence of operational and recruitment-related challenges, as well a lack of codified regulations to drive the development of drugs for pregnant and lactating women, are some of the reasons that could explain the low enrolment rate of pregnant women in clinical trials. These complexities have reinforced the absence of clinical studies to evaluate the safe and efficacious use of drugs during lactation and pregnancy.

FUNCTIONS OF ICMR:



- Provides financial assistance to promote biomedical and health research.
- Proposals in fundamental/ strategic research, development and evaluation of a tool, clinical and operational research are considered for ICMR support.
- It provides assistance by way of grants to scientists in regular employment in the universities, medical colleges, postgraduate institutions, recognized research and development laboratories and NGOs.
- ICMR also provides international fellowship programme for research and training and exposure of Indian biomedical scientists in various countries as well as offering opportunities to scientists from developing countries to come and work in Indian institutes/laboratories.

What is a CSR?

- A CSR is a comprehensive integrated report of a clinical study of any therapeutic, prophylactic or diagnostic agent in which the clinical and statistical description, presentations and analyses are provided in a single report, incorporating tables and figures into the main text of the report and in appendices.
- Provides an explanation of how the critical design features of the study were chosen, information on the plan, methods and conduct of the study.
- Includes efficacy and safety data.
- Represents the most complete synthesis of the planning, execution, and results of a clinical study.

CRO CONTRACT RESEARCH ORGANIZATION

Contract Research Organization (CRO): a company that provides support to the pharmaceutical, biotechnology, and medical device industries in the form of research services outsourced on a contract basis. A CRO may provide such services as biopharmaceutical development, biologic assay development, commercialization, preclinical research, clinical research, clinical trials management, and pharmacovigilance. CROs are designed to reduce costs for companies developing new medicines and drugs in niche markets. They aim to simplify entry into drug markets, and simplify development, as the need for large pharmaceutical companies to do everything 'in house' is now redundant.



Introduction

- The Investigator's Brochure (IB) is a compilation of the **clinical and nonclinical data on the investigational product(s)** that are relevant to the study of the product(s) in human subjects.



Purpose

- Its purpose is to provide **Information to the Investigators** and others involved in the trial such as the dose, dose frequency/interval, methods of administration: and safety monitoring procedure.
- The IB also provides insight to support the clinical management of the study subjects during the course of the clinical trial.