Clinical Trial Process - extra

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1. Role of Sponsor & Regulatory Authority

- **Sponsor**: The company, organization, or institution responsible for developing a new drug or treatment.
  - Example: Pfizer developed the COVID-19 vaccine as a sponsor.
- **Regulatory authority**: Approves drugs before they reach the market.
  - Example:
    - **FDA** (Food and Drug Administration, USA)
    - **EMA** (European Medicines Agency, EU)
    - **DCGI** (Drug Controller General of India, India)

Process flow:
Sponsor develops drug → Applies to FDA → Provides evidence of **safety and efficacy** → FDA reviews → If positive, FDA **approves** → Drug goes to market.

2. Why Clinical Trials?

Drugs must be tested on **human volunteers (subjects)** to confirm:

1. **Safety** → Is the drug safe for humans?
2. **Efficacy** → Does the drug work as intended?

Example:

- A cancer drug may shrink tumors in animals, but it needs to be tested in humans to confirm safety and effectiveness before use.

3. Key Participants

- **Subjects (patients/volunteers)**: People receiving treatment or placebo.
- **Investigators**: Doctors/researchers conducting the trial at sites.

4. Protocol Development

The **protocol** is like the "blueprint" for the study. It details:

- **Title of the study** → e.g., "A Phase III Randomized Controlled Study of Drug X in Hypertension."
- **Purpose/objective** → To evaluate whether Drug X reduces blood pressure.
- **Study population** → Adults aged 18–65 with high blood pressure.
- **Inclusion criteria** → e.g., BP $\geq$ 140/90, no prior treatment.
- **Exclusion criteria** → e.g., pregnancy, liver disease.

Why important?
It ensures trials are done ethically, safely, and scientifically.

5. Bias Avoidance: Randomization & Blinding

- **Randomization** → Assign subjects randomly into groups to remove selection bias.
  - Example: 20 subjects → 10 get Drug X, 10 get placebo.
- **Blinding** → Avoids psychological or investigator bias.
  - *Single-blind*: Subject doesn't know treatment.
  - *Double-blind*: Both subject & investigator don't know.
  - *Open-label*: Both know (used in some special cases).
- **Placebo** → A "fake" drug (like sugar pill) with no active ingredient, used for comparison.

6. Study Designs

- **Parallel group**: Two groups (Drug X vs Placebo), run at the same time.
- **Crossover**: Subjects switch between treatments after a washout period.
- **Multicenter trial**: Conducted at multiple hospitals or countries for diversity.
- **Comparator study**: Investigational drug compared with existing approved drug.

7. Study Stages

1. **Pre-study**
   - Screening (eligibility check).
   - Example: Only patients with HbA1c > 7 are enrolled in a diabetes trial.
2. **Study period**

- **Screening phase** → Select eligible subjects.
- **Treatment phase** → Subjects receive treatment(s).
  - Example: Trt1 = low dose, Trt2 = medium dose, Trt3 = high dose.
- **Follow-up phase** → Monitor safety after stopping treatment.
- *Rule*: No two elements should overlap.
- **Epoch**: Combination of multiple elements (e.g., all Trt phases together).

3. **Post-study**
   - Close-out and preparation of final reports.

8. Visits & Assessments

- **Scheduled visits** → Predefined in protocol (Visit 1, Visit 2, etc.).
- **Unscheduled visits** → Extra visits (e.g., if patient reports side effects).

Example schedule:

Visit	**V1**	**V2**	**V3**	**V4**
Demographics (DM)	X			
Lab tests (LB)		X		
ECG			X	
Vital signs (VS)	X	X	X	X

9. Clinical Data Management (CDM)

- **CRF (Case Report Form)**: Used to collect subject data.
  - *Paper CRF* → Physical forms.
  - *eCRF (Electronic CRF)* → Collected through systems like Medidata Rave.
- **Data Managers**:
  - Validate data (edit checks).
  - Prepare clean datasets for analysis.

10. Biostatistics & SAS Programming

- **Biostatisticians**:
  - Prepare **SAP (Statistical Analysis Plan)**, defining how data will be analyzed.
  - Example: "Compare mean BP reduction between Drug X and placebo using t-test."
- **SAS Programmers**:
  - Generate **TLFs (Tables, Listings, Figures)**.
  - Example:
    - Table → Mean BP reduction at Week 12.
    - Listing → Individual subject adverse events.
    - Figure → Kaplan–Meier survival curve.

11. Medical Writing

- **Medical writers** prepare reports like:
  - **Synopsis** of study results.
  - **CSR (Clinical Study Report)** = Complete trial results submitted to FDA.

12. Population Flags

Different subject groups are defined for analysis:

1. **Enrolled** → Signed Informed Consent Form (ICF).
2. **Screen failures** → Failed screening.
3. **ITT (Intent-to-Treat)** → All subjects who pass screening.
4. **Safety population** → Subjects who took at least one dose.
5. **Per-Protocol** → Subjects with **no major protocol deviations**.
6. **Excluded** → Subjects with protocol deviations.

Example:

- A subject signs consent → enrolled.
- Fails lab test → screen failure.
- Passes screen → ITT.
- Takes drug → safety population.

- Completes trial without deviation → per-protocol.
- If subject missed 3 visits → excluded.