Responsible clinical monitoring of research implementation

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Clinical Trial Stakeholders

Product manager

Clinical Coordinator

DSMB

Data Management

Clinical monitor

Principal investigator

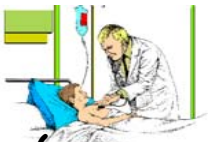
Ethics Committee
(communication approval of documents; report AE acc'ing to SOPs, progress, amendments, etc.)

Institution authorities
(facilities, resources, staff, finance management, policies etc.)

Regulatory authorities
(approval when required, inspection, report SUSARs, etc.)

Ministry of Health
(rotation of staff, procedures allowed in health facilities, etc).

Patients, guardians, sub-investigators, nursing and laboratory staff, health workers



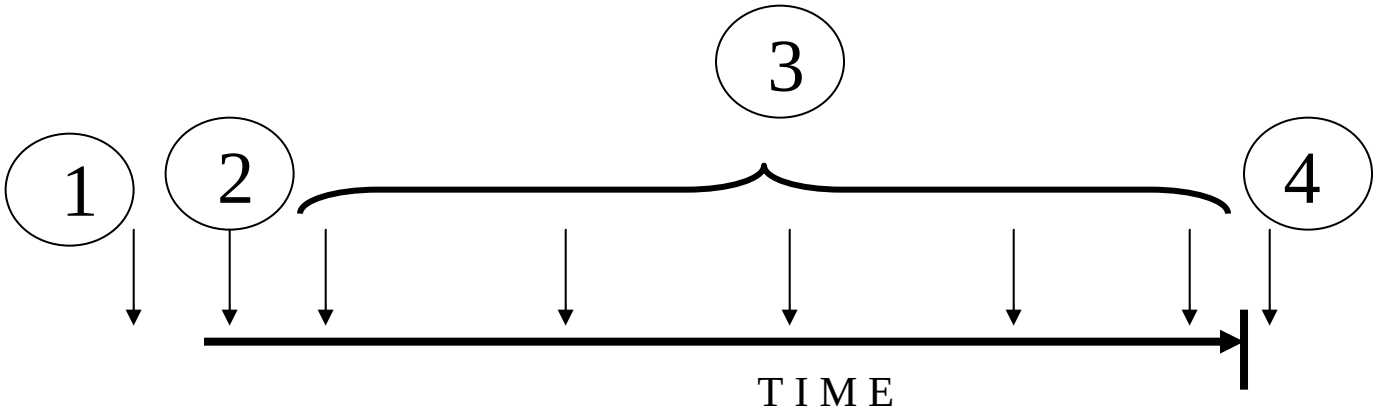
(Recruitment; process of informed consent,follow up, diary cards, medical management, delegation of specific tasks, drug storage, administration, assessment of response, management and reporting of AEs, specimen collection,laboratory pre- during and post-analytical procedures, laboratory quality control etc.),

Responsible clinical monitoring

- Ensures that a trial is conducted, recorded, and reported in accordance with the protocol, standard operating procedures (SOPs), good clinical practice (GCP), and the applicable regulatory requirement(s).
- Indirectly, ensures the application of ethical principles in the conduct of clinical trials

Ethical principles	Areas of application in a clinical trial
Autonomy	Informed consent
Justice	Selection of participants (inclusion and exclusion criteria)
Beneficence	■Research design ■Benefits >> risks
Non-maleficence	■Adequate facilities at the site ■Available and proper medical care during the trial ■Management of adverse events ■Patient confidentiality

Monitoring visits during a clinical trial



1. Pre-trial
2. Initiation
3. Routine monitoring visits
4. Close-out visit

Premises

- Clinical monitor is knowledgeable of trial documents (as much as, and even more, than investigator)
- Clinical monitor is knowledgeable of the local regulations and applicable ones
- Trial documents have been given written approval by the ethics committee
- Clinical monitor is knowledgeable of research ethics and is aware of ethical issues that may arise in the course of the trial monitored

Valid informed consent

- Choice is not only informed but also understood
- Choice is responsible (i.e., patient/ subject/ participant takes the responsibility of his/ her choice)
- Choice is voluntary

Documentation of informed consent

- Written consent form and information sheet are the versions approved by the IRB
- Signed and dated by the subject or subject's legally authorized representative
- Copy given to the person signing the form
- Independent witness and person obtaining informed consent signed the form
- Consent is obtained at the point in time specified in the approved protocol
- Informed consent is renewed when significant changes in the conditions or procedures of the research or if new information becomes available that could affect the willingness of subjects to continue to participate

Monitoring findings

- Informed consent documents are not updated versions
- Information in the informed consent form is incomplete
- The informed consent form is missing
- Definition of legal guardian and witness are not clear
- Point at which informed consent is taken does not comply with approved protocol

Monitoring Justice

- Participants meet all of the inclusion criteria and do not possess any of the exclusion criteria
- Screening is documented and source documents are available for review

Monitoring findings

- Subjects are intentionally made eligible for enrolment
  - Raising Hb levels through blood transfusion
  - Repeating blood chemistry tests
- Screening period is prolonged and delays start of treatment
  - Recruiting in remote areas and participant travels/ transferred to town or a central clinic
  - Waiting for results of blood examinations
  - Obtaining informed consent in a busy clinic
- Some exclusion criteria are waived
  - Serum K+ level of 3.2gm/dl (normal is 3.5)
- Source documents are missing and data/information cannot be validated

Monitoring beneficence

- Investigator, the study team and and new staff are qualified
- Essential documents before the start of, and during the trial are maintained
- SOPs are followed and revised or renewed when needed
- Randomization and blinding are maintained
- Product administered correctly
- Laboratory follows and maintains GCLP
- Local regulations and EC/IRB policies followed

Monitoring non-maleficence

- Resources are adequate to manage medical condition/s and AEs
- Investigator's brochure is on site and updated
- Adverse events (particularly SAEs) are recognized, reported and acted upon promptly and according to the protocol, ICH-GCP and EC/IRB SOPs
- Participant follow-ups are ensured; lost to follow up and withdrawal of consent are documented
- Participant's confidentiality is maintained

Maintaining participant's confidentiality

- Study files and documents are kept in a safe and secure place
- Subject's files are filed individually and kept separate from study files
- Subject's identification is limited to the least number of documents (e.g. screening and enrolment log)
- Area to archive and store study documents in a safe and secure place

Monitoring findings

- Investigators and staff are not well trained or qualified
  - Trail-related procedures
  - Product administration
  - AE management
- Inadequate facilities
  - No pediatric blood pressure apparatus
- Study room is PI's office which is shared with other physicians
- No documentation of Ethics Committee monitoring the trial
  - Correspondence regarding progress reports and renewal of approval
  - Response to reported SAEs
- Errors, misconduct, fraud - carelessness? Intentional?

Empowering clinical monitors for responsible monitoring of clinical research

- Skills and training
  - GCP refresher courses and updates
  - Research ethics and updates
  - Attendance to relevant conferences
- Effective communication
  - With other clinical monitors
  - With sponsors
  - With investigators
- Coordination and team work

Responsible clinical monitoring ensures observance of ethical principles while meeting GCP standards


Thank you!
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