THE INVESTIGATOR’S RESPONSIBILITIES

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Definition

- A group of people working together in a **systemic and scientific manner** to establish facts

- Committed to applying the principles of **GCP** in the conduct of clinical research that may have an impact on the safety and well-being of human subjects (study participants)

- Conducts the clinical trial at a trial site. The **leader of a team may be called the principal investigator**
The Investigator (Research Team)

Some useful terms

- **Investigator/Institution**
  The investigator and/or institution, where required by the applicable regulatory requirements

- **Investigator’s Brochure**
  A compilation of the clinical and nonclinical data on the investigational product, which is relevant to the study

- **Sub-investigator**
  A member of the clinical trial team designated and supervised by the investigator at a trial site perform trial related procedures
The Investigator - Qualifications

Qualifications

- An appropriately qualified person in the relevant field of health care (MD, PhD, nurse)

- Trained and experienced in clinical research

- Familiar with the study (background, study design....) and its requirements
Prerequisites

- Familiar with the background of the study (e.g. disease, management of the disease, treatment with its side effects)

- Familiar with the study – the protocol document and study procedures

- Remember – knowing the literature is fundamental if you want to be an effective and successful investigator

- Allow monitoring by Sponsor
The Investigator - Responsibilities

Responsibilities

- Obtain IRB approval of the protocol and informed consent prior to the initiation of the study and patient enrollment.

- Be familiar with any national laws that may impact the study designs or participation:
  - Drug approval
  - Importation of drugs (where, how, who, costs...)
  - Human tissues (storage, use, transfer to another institution or other country, methods applied...)
  - Funding policies or rules
Resources

- Provide retrospective data to show a potential for recruiting the required number of suitable subjects within the agreed recruitment period

- Sufficient time to properly conduct and complete the trial within the agreed trial period

- Adequate number of qualified staff and adequate facilities

- All persons assisting with the trial are adequately informed about the protocol, the investigational products, and their trial related duties and functions
Medical Care During Study Participation

- A trial related physician should be responsible for all trial related medical decisions

- Adequate medical care for any adverse event

- Inform the subject´s primary physician about the subject´s participation in the study if the subject agrees to the primary physician being informed (recommendation)

- Make a reasonable effort to ascertain the reason for interruption of participation of individuals (medical reasons?)
Before initiating a trial, the investigator should have written and dated from the IRB/IEC for:

- The trial protocol
- Written informed consent form
- Subject recruitment procedures
- Any other written information to be provided to subjects

Provide Investigator’s Brochure and Updates to the IRB/IEC

During the trial the investigator/institution should provide to the IRB/IEC all documents subjects to review
Always conduct the trial in compliance with the protocol

Do not implement any deviation, or changes of the protocol without agreement by the sponsor and EC

Document and explain any deviation from the approved protocol

EXCEPT: immediate hazard to study participants
Drug Accountability

- Drug accountability at the trial site is investigators task
  - Assign drug accountability to an appropriate pharmacist (supervision of the investigator)
  - Store drug as specified, use the drug only in accordance with approved protocol, explain correct use of the study drug to each participant
  - Maintain records (date, quantity, batch number etc.) of:
    - Drug’s delivery
    - The inventory at the site
    - The use by each subject
    - The return to the sponsor or disposition
The informed consent form describes to the signer that with this certain activity, that they are voluntarily taking part of certain risks that come with the activity, and that by signing the form they acknowledge and understand that fact.
Informed Consent

- Informed consent is a “process” – it does not end with the signature of the patient on a piece of paper.

- On-going and interactive process between the research team and the patient:
  - To ensure patient understands the study
  - To ensure patient understands what is required to participate in the study

- Obtain informed consent from patients or parents of minor patients:
  - Prior to starting protocol treatment
  - Prior to randomizing patients if the study is a randomized trial
Informed Consent – Investigator responsibilities

Responsibilities

- Provides necessary information to the patient or parent of a minor child about the study

- Obtain the informed consent (documentation that the process took place)

- May “delegate” to other members of the research team if they are knowledgeable about the informed consent
Informed Consent – Information to be conveyed

Information

- Participation is voluntary
- Information about the patient’s disease
- Rationale for specific therapy planned in the trial
- Description of the research objectives
- Differentiation between research elements and “standard care”
Informed Consent – Information to be conveyed

Information

- Patient’s “required involvement”
  - Duration of participation
  - Frequency of hospitalization, outpatient visit during treatment
  - Frequency of visits after treatment

- Alternative approaches to treatment
  - Standard treatment
  - No treatment if no alternatives exist

- Risks or discomforts (side effects of treatment and procedures)
Informed Consent – Information to be conveyed

**Information**

- State how patient’s confidentiality will be maintained
- Provisions for research-related injuries and compensation for disability or death
- Costs to the patient as a result of participation
- Contact details for problems or question
  - PI
  - Patient advocate
• Document what you do, otherwise it’s considered not to be done!

• But also do what you document!
CRF Handling

CRF (clinical research form)

- Ensure accuracy, completeness, legibility and timeliness of CRFs

- Be consistent with the source documents or explain discrepancies

- Change or corrections to a CRF
  - Should be dated, initialed
  - Explained (if necessary)
Safety

- Report serious adverse events (SAEs) immediately to the sponsor except for those SAEs that the protocol or other document (e.g. Investigator’s Brochure) identifies as not needing immediate reporting. Reports should be followed promptly by detailed, written reports.

- Report unexpected serious adverse drug reactions to the regulatory authority and the EC (SUSARs)
End of Study

- **Premature Termination or Suspension of a Trial**
  - Could be done by Sponsor, Investigator
    - Promptly inform the trial subjects and assure appropriate therapy and follow up
    - Inform sponsor, EC, regulatory bodies

- **End as planned**
  - Final report (is not the same as the publication)
    - Provide the IRB/EC with a summary of the trial’s outcome, regulatory authorities as required
Responsibilities of the Investigator

Delegation
- May delegate responsibilities to other members of the research team
- Associate or Co-Investigator
- Study Coordinator
- Research nurse
Delegation of Responsibilities

Supervision

- **Supervision of the delegated work is essential**
  - Informed consent process and procedures
  - Quality and accuracy of the data recorded on study case report forms

- **Supervision of the care delivered by the staff responsible for the patient is essential**
  - Adherence to the protocol treatment plan
  - Appropriate supportive care
  - Intervention when adverse events occur
The investigator should strive to meet the high standard of GCP in order to provide public assurance that

- Rights, safety and well-being of patients are PROTECTED
- Data is ACCURATE
- Reported results are CREDIBLE