



Clinical Trial Management Society Hungary

Guidance on Principal Investigator responsibilities

I. Supervision of the conduct of a clinical trial:

The Principal Investigator (PI):

- commits her/himself to personally conduct or supervise the clinical trial,
- is responsible for providing adequate supervision of those to whom tasks are delegated,
- is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study.

II. What is adequate supervision?

- Principal Investigator: who has supervisory responsibilities for the Site.
 - A Sub-Investigator should report directly to the Principal Investigator.
- The primary supervisory responsibility should not be delegated.
- Sufficient time to supervise.
- Appropriate level of supervision.

III. Factors that may affect proper oversight:

- Inexperienced Site staff;
- Non-study related workload;
- Complexity of the clinical trial(s);
- Large number of patient population (standard of care);
- Multiple, parallel study conduct;
- Seriously ill patient population concurrently;



- Multiple Site locations or Institutions under the oversight of a single Principal Investigator (“flying PI”);
- Number of subjects enrolled and their statuses (in screening, under treatment, discontinued, in follow-up, etc.).

IV. Plan for appropriate oversight:

- The Principal Investigator should develop a plan to ensure the appropriate supervision and oversight of the clinical trial.
- Routine meetings with staff to review trial progress.
- Routine meetings with the Sponsor’s (or delegate’s) Monitors.
- A procedure for:
 - the timely correction and documentation of issues identified by Study personnel, Monitors, Auditors, or other parties involved in the conduct of the clinical trial,
 - documenting or reviewing the performance of delegated tasks in a satisfactory and timely manner,
 - timely resolution of data queries and discrepancies identified by the study Monitor.
- Risk Based Quality Management (RBQM) from the Sponsor’s side also contributes to efficient PI oversight.

Centralized monitoring simultaneously draws attention to possible errors and flags the issues, while remote monitoring ensures continuous and effective communication with the Sponsor via the responsible Monitor. This also makes issue management and resolution much more efficient and easier for the PI.

- Newsletters containing study/data status based on validated system reports, issued by the Sponsor.

V. Examples for evidence of Principal Investigator’s proper oversight (non-exhaustive list):

- PI approved the Site Standard Operating Procedures (SOPs) to ensure adherence to Good Clinical Practice (GCP) and local regulatory requirements,
- Site staff meeting minutes with a documented confirmation of the PI’s attendance,
- Documented presence at the Initiation visit (Initiation Visit Report [IVR], Training log),
- PI delegated tasks and responsibilities to qualified and trained personnel and this delegation is adequately documented,
- Timely and appropriate management of the study Delegation log (e.g., delegating or stopping study personnel, updating list of delegated tasks, etc.),
- Documented presence at Monitoring visits or availability for monitoring visit related verbal follow-up discussion (Monitoring Visit Report, Contact Report),
- Supervision of third parties and other departments (e.g., Radiology, Pharmacy, etc.) involved in the conduct of the study,
- Follow-up letters addressed to the PI with documented acknowledgement (Follow-up letter signed and dated as confirmation for the review),
- Review and documented acknowledgement of safety information issued by the Sponsor (e.g., safety letters),
- PI is involved in issue management (awareness, resolution, prevention),
- Personal involvement in patient selection (recruitment, review of eligibility), informed consent process (PI signature on the Informed Consent Form), medical source notes signed by the PI (e.g., timely review and evaluation of imaging reports or laboratory results prior to Investigational Product administration and/or medical treatment decisions),
- Evidence of data review (e.g., documented oversight in the electronic Case Report Form [eCRF] system),
- PI is also a treating Investigator of any subject within the study,
- PI attended or supervised any subject visit, and this is documented,
- Documented communication between PI and the Local Ethics Committee (Institutional Research Ethics Committee = Intézeti Kutatásetikai Bizottság, IKEB),
- Therapeutic Area specific meetings (e.g., “onco team” meeting) in the Institution, where further treatments are discussed,
- PI led trainings (refresher after Investigator’s Meeting, brief GCP training).