Implications for monitoring from inspections of investigator initiated trials – the Swedish experience

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Swedish Legislation

- GCP (Nordic Good Clinical Trial Practices) was introduced in Swedish legislation April 1991.
- GCP (ICH GCP) was introduced in Swedish legislation November 1996.
- Legislation 1996 clearly required same quality for Investigator Initiated Trials as for sponsored studies.

Swedish Legislation

- The sponsor should ensure that there exist written, functional procedures for quality control (monitoring) and quality assurance (auditing), that they are followed and that required follow up are conducted within the frame of these procedures and that they are documented.

Investigator Initiated Trials

- 20-25 % of all clinical trials in Sweden are Investigator Initiated Trials.
- Vast majority of these trials conducted at the University Hospitals

Requirements of the Investigator

- Medical Doctor (or Dentist)
- Specialist
- Documented experience of clinical trials
- Documented knowledge of scientific methodology
- Documented knowledge in GCP

Clinical Research Support organisation

- All University Hospitals have a clinical research support organisation that provides support for:
  - protocol writing
  - data management
  - monitoring
  - statistics
  - training and education
  - etc.

Research Nurses

- Each major department has appointed Research Nurses
- Research Nurses
  - specialist position
  - specifically training in clinical trials
  - dedicated work with clinical trials
  - networking group or research nurses both within Sweden and the local hospital

Research Nurses

- Each study has at least one dedicated research nurse involved
- Monitoring usually conducted by a research nurse from another department
- Investigators and departments “borrow” resources from each other

Inspection Strategy

- Inspect sponsored studies
- Inspect investigator initiated studies
- Training and education
- Networking with academic centre
- Networking with research nurses

Quality expectations
Investigator initiated versus commercial

- Same
  - Staff and organisation
  - Applications to EC and RA
  - Informed consent process
  - Conduct of study
- Reduced
  - Monitoring
  - Source data verification
- Limited
  - IMP documentation
  - Laboratory documentation

- Is the quality of Investigator Initiated Trials similar to Pharmaceutical company sponsored studies?
  - scientifically – yes
  - patient safety - yes
  - patient integrity – no
  - GCP - no
  - documentation - no

Inspection findings in IITs

- Violation of patient integrity
  - revealed information
  - incorrect patient information
- Incomplete source data
- Incomplete drug accountability
- Lack of essential document

Inspection findings in IITs

- Lack of quality control
  - No monitoring at all
  - Late introduction of monitoring
  - No SOPs for monitoring
  - Unclear status of monitor
  - Untrained monitor
  - Monitoring reports lacking
  - Findings not followed up

Conclusion

- Investigator Initiated Trials do require quality control (monitoring)

  - but the level, detail and frequency should be tailored to each individual study and a pragmatic and practical approach should be used.