ECETOC’s concept for quality assurance of new technology data considering GLP requirements

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Good Laboratory Practice (GLP)

- OECD Principles on Good Laboratory Practice (as revised in 1997)
  - GLP principles were developed to promote the quality and validity of non-clinical safety data because of serious data manipulation issues
  - basis for corresponding national GLP-regulations in most countries
  - GLP status is prerequisite for mutual international regulatory acceptance of non-clinical safety data!
Basic GLP Principles

- Organizational aspects
  - e.g. independent quality assurance

- Complete (study) planning in advance
  - Standard Operating Procedures (SOP) system, study plan

- Final report must reflect raw data
  - Raw data recording, processing and integrity

- Archiving
  - Full retrospective reproducibility of studies
Organisational aspects

- GLP functions
  - Test Facility Management
  - Study director(s)
  - Quality Assurance Staff
    - Control of GLP compliance by means of inspections
    - to be independent from laboratory
  - Archivist
SOP System
should comprise ...

- General study-related processes
  - Planning, conduct, reporting, archiving of studies
  - e.g. general analytical procedures / data processing
    - Standardization required
    - Scientific data assessment is up to study director (usually not coverable by SOPs) – but should be plausible

- Laboratory/equipment preconditions
  - e.g. calibration schedules, tolerance limits, ...

- Quality management system
Study plan

- Defines study specific details
  - Test item, concentrations, sampling, study specific methods, statistics, ...

- Complete study planning in advance
  - No “inofficial” experiments
  - Planned changes to be defined/justified in study plan amendment
  - Non-planned incidents to be assessed
Data recording - Raw data

= all original records and documentation resulting of the original observations and activities“

- To be defined for each data recording system
  - Essential task, raw data must not be susceptible to manipulation
  - e.g. initially obtained chromatograms

- Paper or electronic raw data ?
  - New technologies – huge amount of electronic raw data
Data Processing

- Report data must be reproducible from raw data!
  - Documentation of all relevant processing steps
  - e.g. manual re-integration of chromatograms
  ➢ Could mean a lot of documentation

- Uncontrolled data „manipulation“ impermissible!
  - Initial data entry must not be deleted!
  - All Data changes/corrections to be justified
  ➢ Data recording/processing software should have audit trail
    • If not?
      • Software development?
      • Disabling of data changes practicable?
      • Commitment to and control of „manual“ audit trail?
Validation
Software and procedures

- Do requested functions/specifications work correctly?
  - „Black box“ software validation possible
- Proper data protection / storage ensured?
- Software access control?
- No software administrator rights for users?
- Audit trail function?
...

- Excel Spreadsheets
  - Verification of calculations / protection of calculation cells
  - Highly variable Excel sheets – manual re-check?
Archiving

- Comprises all data necessary for study reconstruction
  - Raw data, derived data, metadata (e.g. method settings/calibration), …

- Electronic data archiving
  - Data lock required
  - Backup copies
  - Regular control of data integrity and readability
  - For new technologies: administration of huge data amounts

- Archiving period depends on national regulations
Summary
Application of GLP-requirements on new technologies

- requires …
  - Administrative efforts (SOP system, standardized planning, …)
  - Resources: QAU, Archiving, …

- is probably most challenging with respect to …
  - Definition of raw data
  - Reproducibility of all results from raw data / archiving
  - Transparent description of all processing steps
  - Validation / audit trail documentation

But even “as GLP-like as possible” procedures are considered to promote reliability of new technology data for, e.g., risk assessment purposes