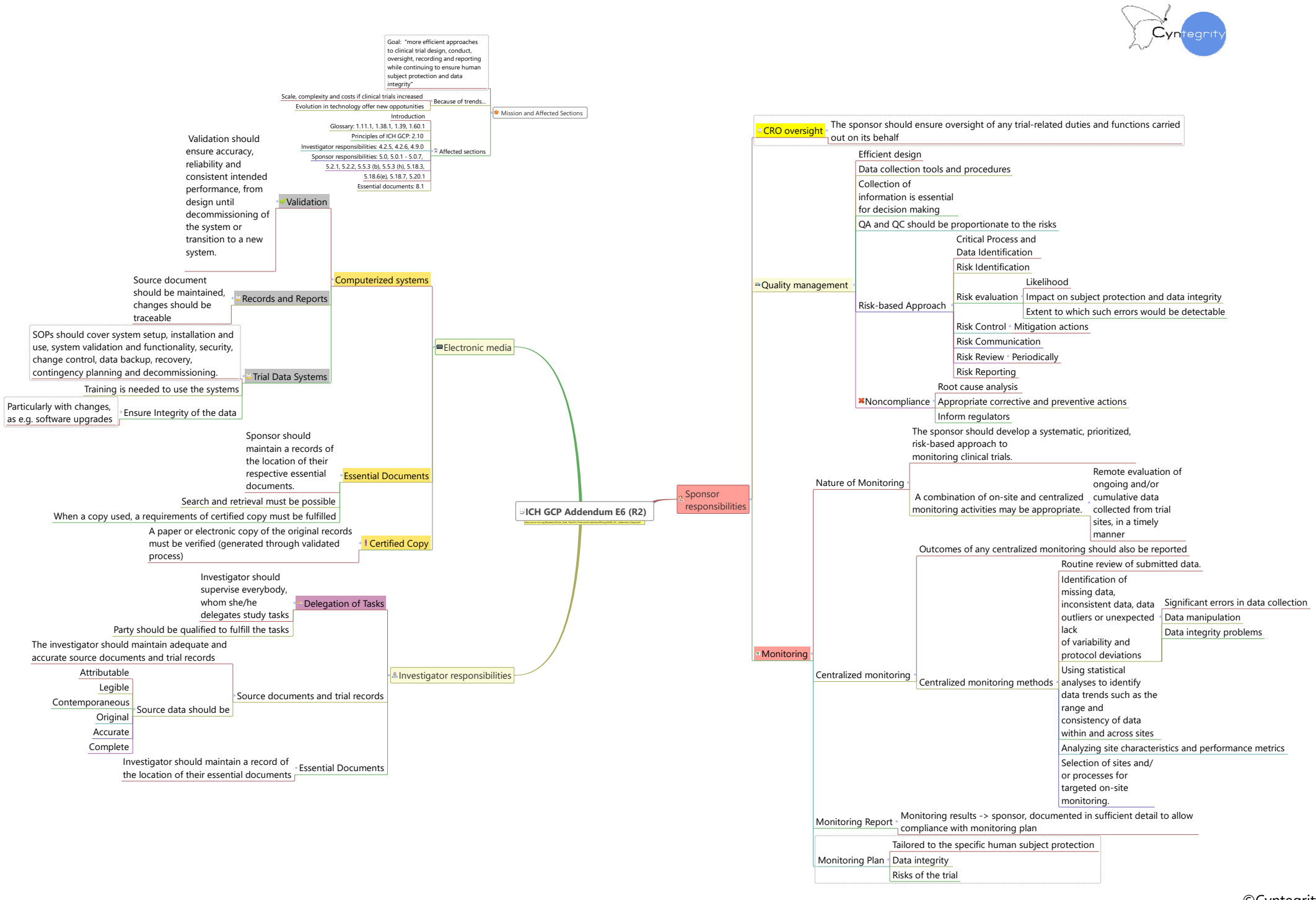
ICH GCP Addendum E6 (R2)
Mission and Affected Sections
Goal: "more efficient approaches to clinical trial design, conduct, oversight, recording and reporting while continuing to ensure human subject protection and data integrity"
Because of trends...
Scale, complexity and costs if clinical trials increased
Evolution in technology offer new oppotunities
Affected sections
Introduction
Glossary: 1.11.1, 1.38.1, 1.39, 1.60.1
Principles of ICH GCP: 2.10
Investigator responsibilities: 4.2.5, 4.2.6, 4.9.0
Sponsor responsibilities: 5.0, 5.0.1 - 5.0.7, 5.2.1, 5.2.2, 5.5.3 (b), 5.5.3 (h), 5.18.3, 5.18.6(e), 5.18.7, 5.20.1
Essential documents: 8.1
Electronic media
Validation
Validation should ensure accuracy, reliability and consistent intended performance, from design until decommissioning of the system or transition to a new system.
Computerized systems
Records and Reports
Source document should be maintained, changes should be traceable
Trial Data Systems
SOPs should cover system setup, installation and use, system validation and functionality, security, change control, data backup, recovery, contingency planning and decommissioning.
Training is needed to use the systems
Ensure Integrity of the data
Particularly with changes, as e.g. software upgrades
Essential Documents
Sponsor should maintain a records of the location of their respective essential documents.
Search and retrieval must be possible
When a copy used, a requirements of certified copy must be fulfilled
Certified Copy
A paper or electronic copy of the original records must be verified (generated through validated process)
Investigator responsibilities
Delegation of Tasks
Investigator should supervise everybody, whom she/he delegates study tasks
Party should be qualified to fulfill the tasks
Source documents and trial records
The investigator should maintain adequate and accurate source documents and trial records
Source data should be
Attributable
Legible
Contemporaneous
Original
Accurate
Complete
Essential Documents
Investigator should maintain a record of the location of their essential documents
Sponsor responsibilities
CRO oversight
The sponsor should ensure oversight of any trial-related duties and functions carried out on its behalf
Quality management
Efficient design
Data collection tools and procedures
Collection of information is essential for decision making
QA and QC should be proportionate to the risks
Risk-based Approach
Critical Process and Data Identification
Risk Identification
Risk evaluation
Likelihood
Impact on subject protection and data integrity
Extent to which such errors would be detectable
Risk Control
Mitigation actions
Risk Communication
Risk Review
Periodically
Risk Reporting
Noncompliance
Root cause analysis
Appropriate corrective and preventive actions
Inform regulators
Monitoring
The sponsor should develop a systematic, prioritized, risk-based approach to monitoring clinical trials.
Nature of Monitoring
A combination of on-site and centralized monitoring activities may be appropriate.
Remote evaluation of ongoing and/or cumulative data collected from trial sites, in a timely manner
Centralized monitoring
Outcomes of any centralized monitoring should also be reported
Centralized monitoring methods
Routine review of submitted data.
Identification of missing data, inconsistent data, data outliers or unexpected lack of variability and protocol deviations
Significant errors in data collection
Data manipulation
Data integrity problems
Using statistical analyses to identify data trends such as the range and consistency of data within and across sites
Analyzing site characteristics and performance metrics
Selection of sites and/ or processes for targeted on-site monitoring.
Monitoring Report
Monitoring results -> sponsor, documented in sufficient detail to allow compliance with monitoring plan
Monitoring Plan
Tailored to the specific human subject protection
Data integrity
Risks of the trial