



Part 3: The Evolution of IT Quality and Validation in Clinical Trials: Understanding ICH E6(R3) GCP Guidelines and Related Regulations

Practical Implementation Strategies

Developing a Comprehensive IT Quality Framework

Organizations conducting clinical trials should develop an integrated IT quality framework that addresses the requirements of ICH E6(R3) alongside other applicable regulations. Key components include:

1. IT Quality Risk Management Process: Develop a formal process for assessing the risks associated with computerized systems in clinical trials and determining appropriate controls.
2. System Inventory and Categorization: Create and maintain an inventory of all computerized systems used in clinical trials, categorized by their impact on participant safety and data reliability.
3. Validation Strategy: Establish a tiered validation approach that applies different levels of validation rigor based on system criticality. Section 4.3.4(e) of ICH E6(R3) acknowledges that "Different degrees of qualification/validation may be needed for bespoke systems, systems designed to be configured or systems where no alterations are needed."
4. Data Governance Framework: Implement comprehensive data governance policies and procedures that address the full data lifecycle from creation to archiving or destruction.
5. Security Management Program: Develop an information security program specific to clinical trial systems, ensuring compliance with ICH E6(R3) and relevant data protection regulations.
6. Training Program: Create a training curriculum for different roles involved in clinical trials, covering both system use and broader regulatory requirements.
7. Audit and Monitoring Strategy: Establish an ongoing monitoring program to assess compliance with IT quality requirements throughout the trial lifecycle

Documentation and Evidence Considerations

ICH E6(R3) places significant emphasis on documentation as evidence of compliance. Organizations should ensure:

1. Documentation is kept current throughout the system lifecycle
2. Documentation is retained as part of the essential records (see Appendix C of ICH E6(R3))



3. Quality records are sufficient to reconstruct activities
4. Electronic records meet the requirements of relevant regulations (e.g., 21 CFR Part 11)

Vendor Management

Many organizations rely on vendors for clinical trial systems and services. ICH E6(R3) addresses this through its requirements for service providers:

1. "The sponsor is responsible for assessing the suitability of and selecting the service provider to ensure that they can adequately undertake the activities transferred to them" (section 3.6.7).
2. "The sponsor should have access to relevant information (e.g., SOPs and performance metrics) for selection and oversight of service providers" (section 3.6.8).
3. "The sponsor should ensure appropriate oversight of important trial-related activities that are transferred to service providers, including activities further subcontracted by the service provider" (section 3.6.9).

Organizations should develop formal vendor qualification and oversight processes that specifically address IT quality and validation requirements.

Looking Ahead: Emerging Technologies and Future Regulatory Directions

AI and Machine Learning in Clinical Trials

As artificial intelligence and machine learning become more prevalent in clinical trials, regulatory frameworks will need to evolve. While ICH E6(R3) does not explicitly address AI validation, the risk-based principles it establishes provide a foundation for validating AI/ML systems.

Organizations implementing AI in clinical trials should consider:

1. How to validate AI algorithms that may evolve over time
2. How to demonstrate the reliability of AI-derived endpoints
3. How to maintain appropriate human oversight of AI systems

The FDA's proposed regulatory framework for AI/ML-based Software as a Medical Device (SaMD) offers complementary guidance for AI systems used in clinical trials.



Decentralized Clinical Trials

ICH E6(R3) acknowledges the growing trend toward decentralized trial elements, noting that "monitoring approaches should consider the activities and services involved, including decentralised settings" (section 3.11.4). The guideline also recognizes various technology-enabled approaches, noting that "Obtaining consent remotely may be considered where appropriate" (section 2.8.1(d)) and that "Varied approaches (e.g., text, images, videos and other interactive methods) may be used in the informed consent process" (section 2.8.1(c)).

Future regulatory updates will likely provide more specific guidance on:

1. Validation of patient-facing technologies
2. Data integrity in home-based assessments
3. Remote source data verification
4. Identity verification in virtual environments

Blockchain and Distributed Ledger Technologies

While not addressed in current regulations, blockchain and distributed ledger technologies are increasingly discussed as potential solutions for clinical trial data integrity. Future regulatory guidance may address:

1. Validation requirements for blockchain-based systems
2. Acceptance of blockchain as a means of ensuring data integrity
3. Integration of blockchain with existing regulatory frameworks

Conclusion

ICH E6(R3), coming into effect in July 2025, represents a significant evolution in regulatory expectations for IT quality and validation in clinical trials. By adopting a risk-based approach and emphasizing the importance of data integrity throughout the data lifecycle, the guideline provides a flexible framework that can accommodate technological innovation while ensuring participant safety and data reliability.

Organizations conducting clinical trials should view ICH E6(R3) as part of a broader regulatory ecosystem that includes 21 CFR Part 11, GDPR, HIPAA, and other relevant regulations. By developing an integrated approach to IT quality management that addresses all applicable requirements, organizations can ensure regulatory compliance while improving the efficiency and reliability of their clinical trials.



DIGITAL QUALITY ASSOCIATES
WHERE EXPERIENCE COUNTS

As clinical trial technology continues to evolve, regulatory frameworks will undoubtedly adapt. Organizations that establish robust, risk-based IT quality systems now will be well-positioned to incorporate new technologies and comply with future regulatory expectations.

The journey toward digital transformation in clinical trials requires continuous attention to IT quality and validation. ICH E6(R3) provides a roadmap for this journey, emphasizing that quality is not just about compliance but about ensuring that clinical trial data reliably supports decisions that affect patient health and safety.

final message?

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