Update to GCP: ICH E6(R3)

Dana Nohynek | Director, Regulatory Affairs & Quality Assurance

ctn+
CIHR Pan-Canadian Network for HIV and STBBI Clinical Trials Research | Réseau pancanadien pour des essais cliniques sur le VIH et autres ITSS

Overview

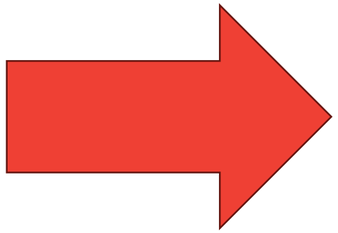
- ICH E6: Good Clinical Practice (GCP) guideline
  - Global standard for designing, conducting, recording, and reporting clinical trials
  - Protect trial participants & ensure data integrity
- Evolution
  - E6(R1) (1996): foundational GCP guideline
  - E6(R2) (2016): introduced risk-based approaches, electronic systems, CRO oversight
  - E6(R3) (2025): flexible, principle-based, adaptable to diverse trial types

R3 Goal: Modernize GCP to reflect advances in clinical trial design, technology, and diversity of data sources

Paradigm Shift

E6(R2): Prescriptive & Rigid

- Checklist-driven requirements
- Site-centric
- Paper-heavy processes
- Monitoring emphasis after trial starts
- Rigid sponsor vs. investigator roles



E6(R3): Principles & Flexibility

- Principle-based, adaptable framework
- Participant-centered
- Embraces technology
- Quality by Design – critical-to-quality factors
- Shared responsibilities with accountability

E6(R3) GOAL: Modernize GCP to reflect advances in clinical trial design, technology, and diversity of data sources

New Format

- Modular, flexible system designed for future updates without rewriting full guideline
- Annex 1: Principles
  - 12 overarching principles of GCP
  - High-level, flexible, adaptable to all trial types
- Annex 2: Application Guidance *(Draft Version 2024 endorsed by ICH members, under public consultation)*
  - More detailed, context-specific guidance
  - Can evolve separately (e.g., different annexes for different trial types)

Key Themes

- Flexibility in Trial Designs
  - Explicit recognition of decentralized and digital trials
  - Accommodates real-world evidence and adaptive approaches.
- Quality by Design (QbD) and Critical to Quality (CtQ) Factors
  - Trials should be designed to focus on critical factors affecting reliability & safety
- Risk Proportionality (NEW)
  - Importance of data being collected
  - Risks to participant safety
  - Reliability of trial results
- Data & Technology
  - Encourages use of electronic records, wearables, and remote data capture
- Roles & Responsibilities (NEW)
  - Investigator & sponsor responsibilities allow delegation and shared responsibilities in innovative trial models.

Critical-to-Quality (CtQ) Factors

- Direct impact participant safety/ rights and data reliability in clinical trial
- Purpose: Focus resources and monitoring on what matters most for trial integrity.
- Examples:
  - Endpoints – accuracy and completeness of key efficacy data.
  - Safety – timely detection and reporting of AEs
  - Informed consent processes – participant understanding and proper documentation.
  - Eligibility – inclusion/exclusion compliance
  - Data integrity – accurate, reliable, and secure data capture
- Implementation:
  - Identify CtQ factors during trial design.
  - Apply risk-based monitoring and oversight proportionate to their impact.
  - Reassess CtQ factors throughout the trial if needed (adaptive trials).

Not all trial elements are equally critical – focus on what most affect safety and reliable results.

Integration of E8(R1):

General Considerations for Clinical Trials

- Quality Risk Management: emphasis on QbD reflects E8(R1) principles, including CtQs
- Trial Design: incorporates E8 guidance on scientifically sound, efficient, and ethical trial design.
- Proportionality & Complexity: Enforces scalable quality practices depending on trial risk and complexity.
- Participant Safety & Rights: integrates E8's focus on participant welfare as key aspect of trial design
- Integrated Trial Management: Incorporates E8 principles of efficient operations and decision-making
- Data Quality & Integrity: Aligns with E8's emphasis on reliable, meaningful data

ctn+

Summary

- E6(R3) modernizes GCP for a digital, diverse trial environment.
- Key paradigm shift is from prescriptive to principle-based, flexible, quality-focused.
- Intent of update is to maintain participant protection and data integrity while enabling innovation in clinical research.
- Health Canada adaption – April 1, 2026

Thank You

Questions? Email dnohynek@hivnet.ubc.ca

ctn+

CIHR Pan-Canadian Network for HIV and STBBI Clinical Trials Research

Réseau pancanadien pour des essais cliniques sur le VIH et autres ITSS