HMRI
Hunter Medical Research Institute

ICH E6 GCP Revision

ARCS Conference 2023 Session Summary

In partnership with our community

THE UNIVERSITY OF NEWCASTLE AUSTRALIA

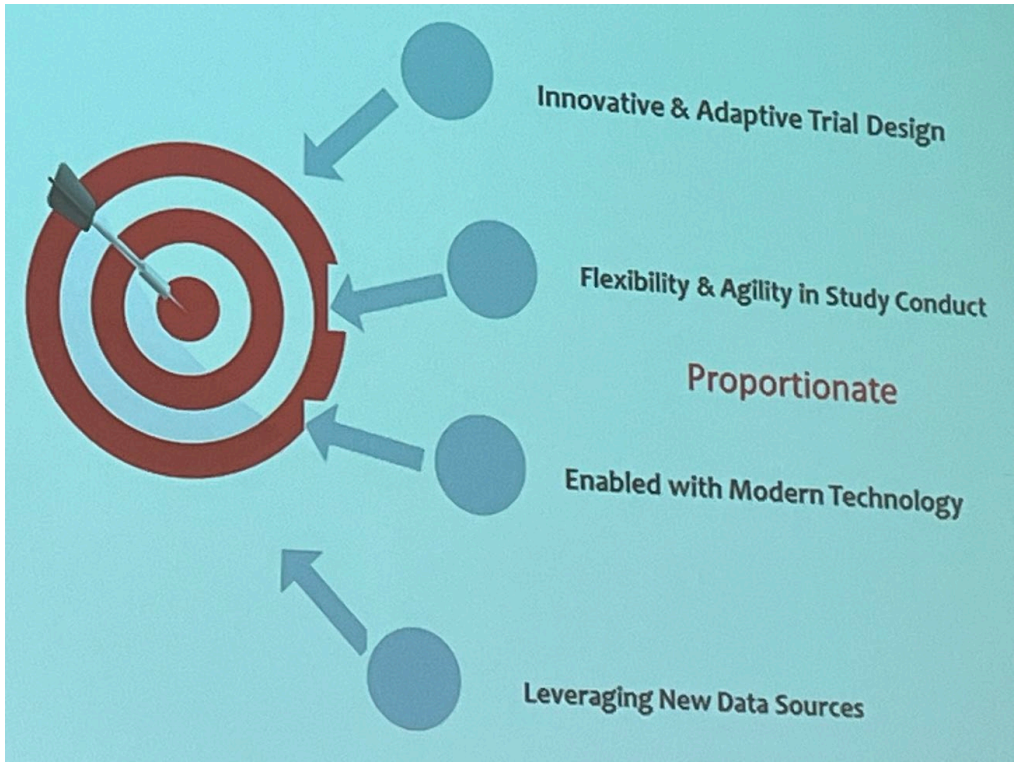
NSW GOVERNMENT Health
Hunter New England
Local Health District

Contents

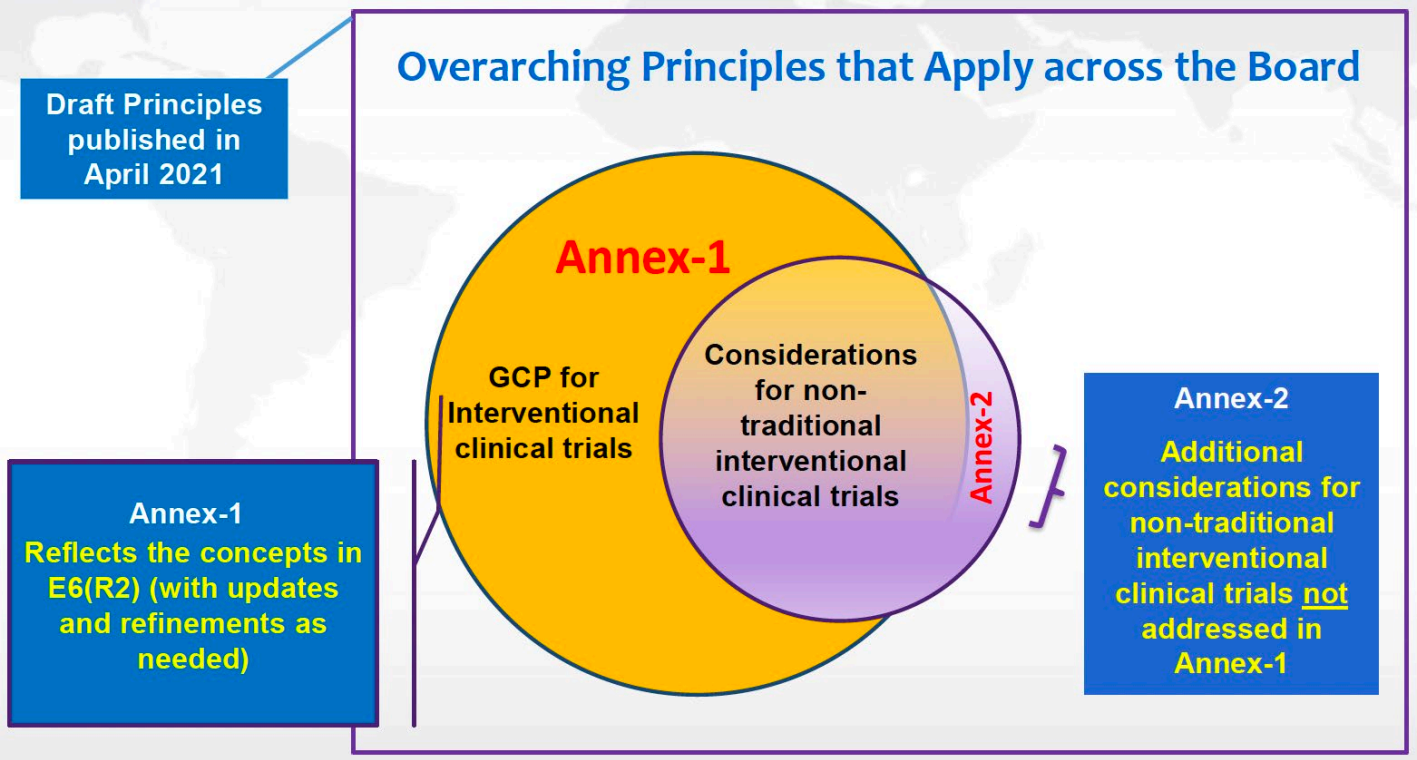
- Why revise ICH E6(R2)?
- Composition of ICH E6(R3)
- Progress of ICH E6(R3)
- Overview of ICH E6(R3)
- ICH E6(R3) Principles
- ICH E6(R3) Substantive Changes

Why Revise ICH E6(R2)?

- Research landscape is changing
- Need to maximise efficiencies to facilitate innovations and clinical trials
- Digitisation of research and healthcare
- Real-world data sources / use of electronic health records



Composition of ICH E6(R3)



R3 will be comprised of:

- an overarching Principles document cont. Annex 1

(proposed draft available here)

PLUS

- Annex 2

Progress of ICH E6(R3) Revision

Overview of ICH E6(R3)

- Substantive Changes:
  - Principles of GCP
  - Annex 1
    - Investigator
    - Sponsor
    - Data governance – Investigator and Sponsor (new)
  - Glossary
  - Appendix C
    - Essential records for the Conduct of a Clinical Trial

- Other Changes
  - Annex 1
    - Institutional Review Board (IRB) / Independent Ethics Committee (IEC)
  - Appendices A & B
    - Investigator's Brochure
    - Clinical Trial Protocol and Protocol Amendments

ICH E6(R3) Principles - New

Risk Proportionality

- Focus on participant safety and reliability of results
- Risks beyond those associated with standard care

Roles and Responsibilities

- Clarification of transfer of activities by the Sponsor and delegation by the Investigator
- Maintenance of appropriate oversight

ICH E6(R3) Principles - Revised

Ethical Principles
- Making sure not to unnecessarily exclude particular participant populations

Informed Consent
- Taking into consideration relevant aspects of the trial

IRB/IEC Review
- Periodic review according to regulatory requirements

Science
- Periodic review of scientific knowledge and approaches

Qualified Individuals
- Individuals with different expertise and training may be needed across all CT phases

ICH E6(R3) Principles – Revised (cont.)

Quality

- The quality and amount of information generated should support good decision-making

Protocol

- A well-designed trial protocol is fundamental to the protection of participants and for the generation of reliable results
- The protocol and other documents for trial execution should be clear, concise and operationally feasible

Reliable Results

- Trial processes should support the key trial objectives
- Clinical trials should incorporate efficient and well-controlled processes for managing
- The transparency of clinical trials with registration on publicly accessible databases and the public posting of CT results

Investigational Product

- IPs should be carefully managed to align with treatment assignment and maintain blinding, where applicable
- IP provided to a trial participant should retain its quality

ICH E6(R3) Substantive Changes - Investigator

Informed Consent

- Varied approaches may be used to provide information and discuss the trial
- Consent may be documented by written or **electronic** signed and dated consent form
- Assent information should be provided to participants who are minors

ICH E6(R3) Substantive Changes - Investigator

Evidence for qualifications

- allows flexibility in type of documentation

Training requirements

- staff should be trained to enable them to fulfill **all** of their delegated tasks, even those that go beyond their usual training and experience

Use of computerised systems

- expectations regarding the use of these systems at site
- data acquisition traceability should be maintained, and participants should be provided with appropriate training
- ensure that ‘incidents’ are reported to the sponsor and, where applicable, to the IRB/IEC.

ICH E6(R3) Substantive Changes - Investigator

Clarification of Expectations

- Regarding service providers and transfer/delegation of tasks
- Around identification and maintenance of source records and timely data review
- Requirements for delegation documentation

ICH E6(R3) Substantive Changes - Sponsor

Monitoring Clarifications

- Monitoring is one of the principal QC activities
- Expectations for centralised monitoring and visits to sites (on-site or remote)
- What the monitoring strategy should consider (purpose, design, blinding, safety profile, endpoints) in a risk proportionate approach.

Investigational Product

- For drug that has already been approved for marketing, alternative approaches may be used.

ICH E6(R3) Substantive Changes - Sponsor

Quality Management

- Clarification of requirements for assessment and management of ‘critical to quality’ factors impacting participant safety or result reliability
- Encourages proportionality
- Clarification on acceptable ranges beyond which deviations could represent systemic issues

Computerised Systems and Data Management

- Clarification on importance of certain processes e.g., blinding and when unblinding may occur
- Computerised systems should be appropriate and risk-based

Sponsor Oversight

- Oversight of other sites is part of the overall QC strategy

ICH E6(R3) Other Changes

Data Governance

- Major revamp resulting in separate section devoted to data governance

Glossary

- Revised terms and new terms

Essential Records

- Guidance on what makes a record ‘essential’
- Clarity on content and maintenance of essential records
- Documents listed in 2 tables – essential records or potential essential records

In Summary

- Intent of revision is to facilitate innovations in clinical trial design and conduct while providing guidance to help ensure participant safety and generation of reliable results.
- Comments on any considerations that may have been missed or any clarifications that may be needed where text is ambiguous is welcomed.
- Details on how to provide your comments on the draft E6(R3) are located on the ICH Public Consultations page (https://www.ich.org/page/public-consultations).