Overview of ICH E6 R3 renovation

MSP Advisory Platform

12 March 2025

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ICH E6 R3 (Principles and Annex 1) EWG Regulatory Chair, Head of Inspections, EMA

European Medicines Agency

- History of ICH E6
- Reasons for change
- Development of guideline
- Overview of main changes
- Implementation

History of ICH E6

E6 - 1996

- Described **the responsibilities of investigators and sponsors** and expectations of interested parties in the conduct of clinical trials;
- Covered aspects of **monitoring, reporting, and archiving of clinical trials**;
- Included sections for **essential documents** and **investigator brochures**

E6 (R2) - 2016

- Included integrated **addendum to encourage implementation of improved and more efficient approaches** to GCP, while continuing to ensure human subject protection; and
- Updated standards for **electronic records**.

E6 (R3) - 2025

- Grounded in the foundational principle of **Quality by Design (QbD)**
- Involves **critical thinking**
- Utilises **proportionate, risk-based approaches**
- Recognises that a **one size does not fit all**.

Reasons for change

Inputs from stakeholders indicated a **need for change**

- Including Clinical Trials Transformation Initiative survey, articles (incl. open letter to ICH and EMA) and regional stakeholder engagement

Concerns about:

- **Rapidly evolving clinical trial ecosystem** not reflected by R2
- Academic community were concerned about a **lack of proportionality**
- R2 guidance was seen as a **“one-size-fits-all” approach**
- **Ability of clinical trials to meet all GCP requirements** in different situations (e.g. during public health emergencies)
- GCP **applied when not applicable**

Development of ICH E6 R3

- **Major rewrite** responding to need for change
- **Stakeholder engagement essential**
  - Expert working group (EWG) comprised of global industry and regulator representatives
  - **Engaged extensively with academic stakeholders** throughout the process
  - Various international and regional workshops (including workshop at EMA in July 2023)
  - **Over 7,000 comments received** during public consultation on principles and annex 1
- Increased transparency during development
  - **Draft principles published in April 2021** along with public web conference in May 2021

Overview of main changes (1)

New structure to provide clarity and better readability.

Included **language to facilitate innovations** in clinical trial design, technology and operational approaches (e.g. media neutrality in documents).

N.B.: **Annex 2** being developed **on alternative trial types and technologies**

Set a **foundation for practical/feasible expectations** (through adoption of QbD and proportionate risk-based approaches) for responsibilities of sponsor and investigator in an evolving clinical trial ecosystem.

Encourage **fit-for-purpose approaches**.

- Proportionality and risk-based approaches with a focus on the clinical trial's **critical to quality factors** (i.e., whose integrity is fundamental to safety of participants and the reliability of trial results);
- **Thoughtfulness** in the **design and conduct**

Overview of main changes (2)

Incorporate **learning from innovative clinical trial designs** and lessons from public health emergencies/pandemics.

Encourage transparency by clinical trial registration and result reporting.

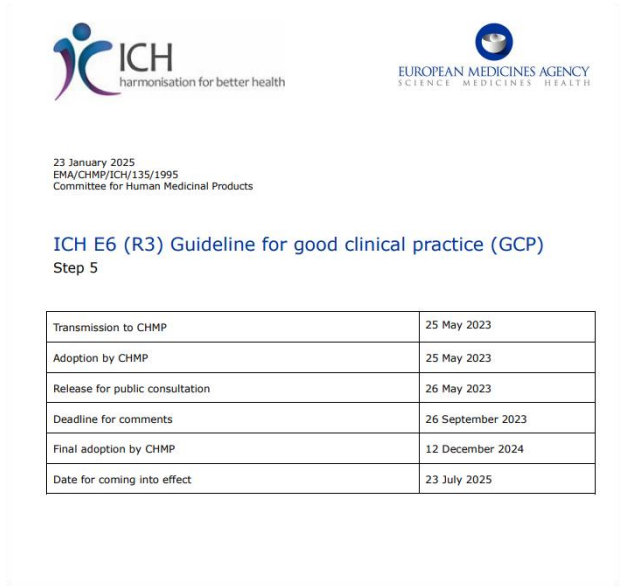
Provide additional language to **enhance the informed consent process**.

New **data governance section** (applicable to investigators and sponsors)

Greater **proportionality added to essential records** appendix

Implementation

- In EU, guideline comes into effect on **23 July 2025**
- **Training!**
  - ACT EU ICH GCP E6 R3 workshop on 19, 20 Feb 2025
    - **2,000 attendees** from 50 countries
    - Overwhelmingly positive feedback
    - Hybrid meeting, recoding online
  - **Online training** being developed at global ICH level
  - Network engaged in **regional workshops**
  - **Training of regulators** (e.g. GCP IWG Cyprus workshop in Oct 2024, more to come)
- **Impact analysis of E6 guideline** against other guidelines/papers



ICH harmonisation for better health

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

23 January 2025
EMA/CHMP/ICH/135/1995
Committee for Human Medicinal Products

ICH E6 (R3) Guideline for good clinical practice (GCP)
Step 5

Transmission to CHMP	25 May 2023
Adoption by CHMP	25 May 2023
Release for public consultation	26 May 2023
Deadline for comments	26 September 2023
Final adoption by CHMP	12 December 2024
Date for coming into effect	23 July 2025

Summary

- **Major rewrite**, responding to technological advances in clinical trials and stakeholder feedback
- **New structure** with a focus on principles, **dedicated data governance section** and new **annex 2**
- All provisions looked at **ensure future proof and strip out unnecessary burden**
- Implementation date in EU **23 July 2025**
- Extensive change management programme – incl. **training** and **impact analysis on guidelines/papers** under way

Thank you

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