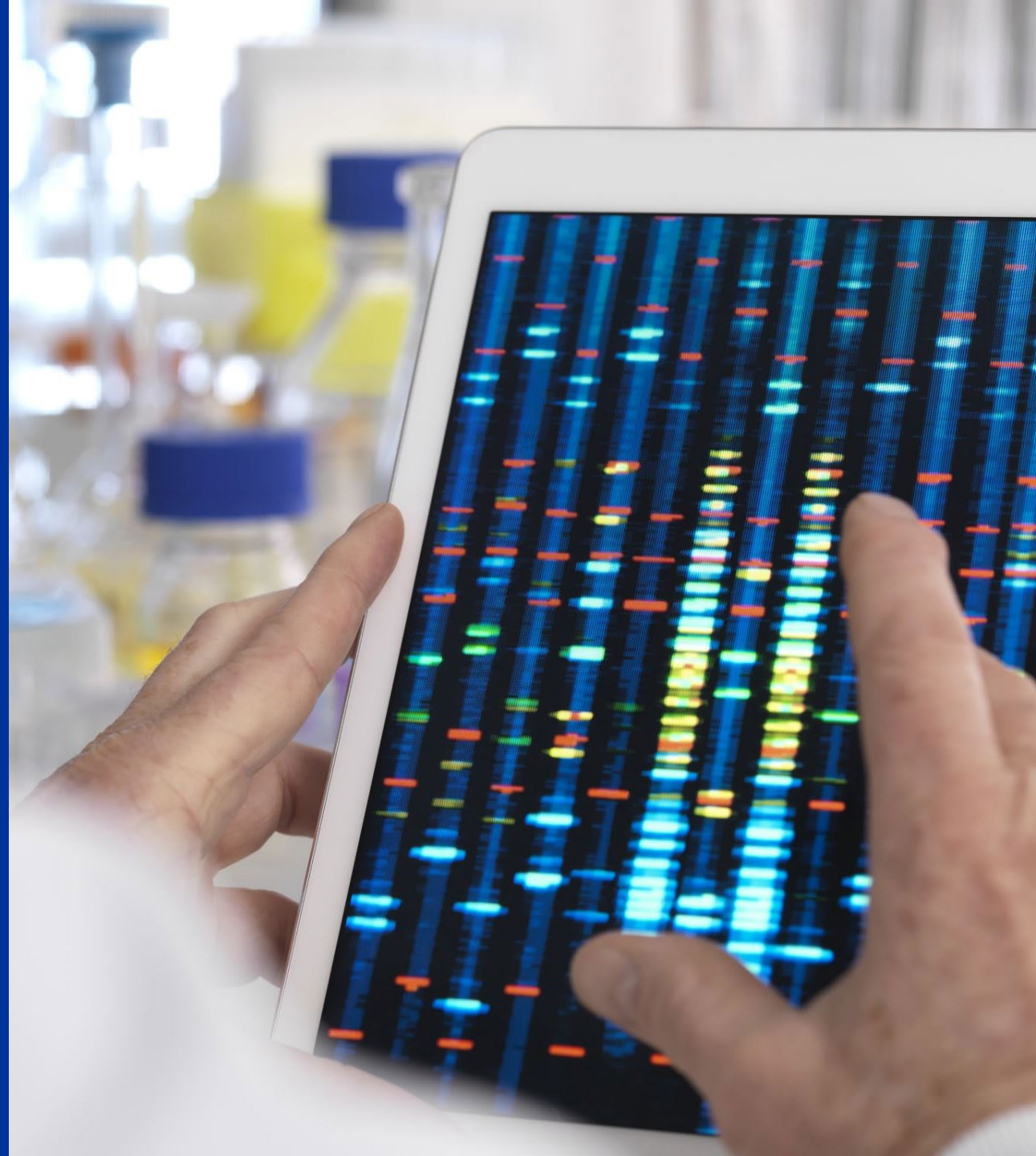
EMA
EUROPEAN MEDICINES AGENCY

Overview of ICH E6 R3 renovation

Peter Twomey

Head of Inspections, EMA and Regulatory Chair, ICH E6 Expert Working Group (Principles and Annex 1).

ENPR Annual meeting, 20 Nov 2025



What we will cover

- What is GCP?
- History of ICH E6 R3
- Reasons for change
- Main changes
  - Revised structure
  - Assent/consent for minors
  - Annex 2
- Implementation

What is Good Clinical Practice?

A **standard** for the planning, initiating, performing, recording, oversight, evaluation, analysis and reporting of clinical trials that **provides assurance** that the **data and reported results are reliable** and that **the rights, safety and well-being of trial participants are protected**.

Globally recognised, reasonably concise

Legal requirement that data from trials submitted as part of MAAs in EU comply with GCP

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**

Overview of main changes (1)

New structure to provide clarity and better readability, focus on principles.

Provide additional **clarity on the scope** e.g. E6 only applies to interventional trials involving medicines.

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**

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

Annex 2 – decentralised and pragmatic elements, use of RWD and electronic health records

Overview of main changes (2)

Two new principles

- Principle 7: Processes should be **proportionate to the risks to trial participants and importance of data**, **avoid unnecessary burden** on participants and investigators
- Principle 10: Clarification of **roles and responsibilities**

Data should be **sufficient** to support decision making =/= perfect

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

Clarity on assent and re-consent

- Requirement for assent for a minor (in line with local requirements) (Principle 2.1 and glosary)
- Information provided should be clear and concise during consenting (Principle 2.2), and for assent, age appropriate information should be provided (Annex 1, 2.8.12)
- A process for consent if the minor reaches adult age during the trial (Annex 1, 2.8.12)
- Legally acceptable representative required, who act on the participant's best interests (Principle 2.1)

New structure

Principles are in the core part of the guideline – **focus should be on their fulfilment**

E6(R3) Guideline

E6(R3) Principles and Annex 1 replacing E6(R2)

I. INTRODUCTION

II. PRINCIPLES OF ICH GCP

III.ANNEX 1

1. Institutional Review Board/Independent Ethics Committee (IRB/IEC)
2. Investigator
3. Sponsor
4. Data Governance – Investigator and Sponsor **(new)**

APPENDICES

Appendix A. Investigator's Brochure
Appendix B. Clinical Trial Protocol and Protocol Amendment(s)
Appendix C. Essential Records for the Conduct of a Clinical Trial

GLOSSARY

ANNEX 2 – *aiming for finalisation (step 4) by end of year/start of 2026*

ICH E6(R3) – Annex 2 Background

Step 2

- Annex 2 provides considerations that focus on examples of trials that incorporate:

Decentralised Elements

Trial-related activities conducted outside the investigator's location

- *E.g., trial visits conducted at participant's home / local healthcare centre / mobile medical units; or data acquisition performed remotely using digital health technologies (DHTs)*

Pragmatic Elements

Those that integrate aspects of clinical practice into the design and conduct of the trial

- *E.g., simplified protocols with streamlined data collection*

Real World Data (RWD)

Include the use of data relating to patient health status collected from a variety of sources outside of clinical trials

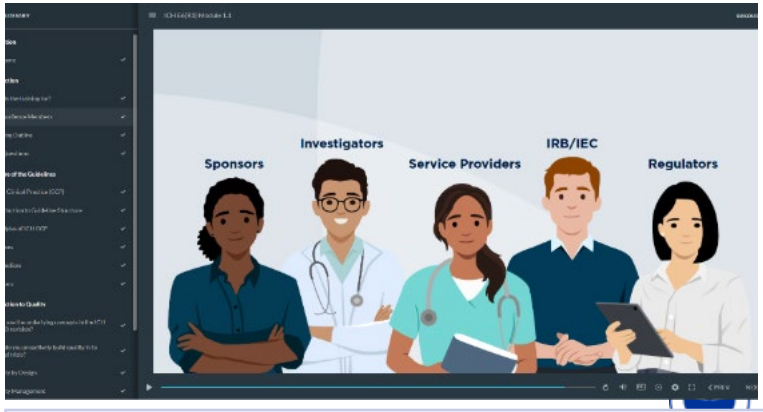
- *E.g., electronic health records (EHRs), registries, claims data*

Implementation

- Principles and Annex 1 effective in EU from **23 July 2025**
- Extensive training available
  - ACT EU Feb 2025 workshop
  - Step 4 ICH presentation
  - Interactive training available on ICH website
- Change control activities:
  - Training of GCP inspectors in Oct 2024 and May 2025
  - Impact analysis of documents that require updates
  - Update to risk-proportionate approaches in CTs (CTCG)

ACT EU Feb 2025 workshop - Amsterdam

GCP IWG Workshop - Cyprus



Interactive training materials – ICH website

Summary

- **Major rewrite of R2**, 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**
- **Two new principles**, focusing on proportionality/risk-based approaches and clarifying roles and responsibilities
- All provisions looked at **ensure future proof and strip out unnecessary burden**
- Important to **read guideline in conjunction with other ICH guidelines** (in particular E8)

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Thank you

peter.twomey@ema.europa.eu

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