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Health Products Regulatory Authority

ICH GCP Revision and EU Clinical Trial Regulation

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Irish Research Nurses Network Annual National Conference

Friday, 17 November 2017

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Overview

- Guideline for Good Clinical Practice E6 (R2)
  - Background/objective
  - Key changes
  - Current status

- Clinical Trial Regulation
  - Background/objective
  - Key changes
  - Current status

Guideline for Good Clinical Practice E6 (R2)

- Integrated Addendum to ICH E6(R1)
- Why needed?
  - Since 1996 adoption of ICH, clinical trials have evolved substantially
  - Approach to GCP needed modernisation to keep pace with scale and complexity of clinical trials and to ensure appropriate use of technology
- Amended to encourage implementation of improved and more efficient approaches to clinical trials
- Addendum supplements ICH E6(R1) with additional text
- Date for coming into effect: 14 June 2017 (EMA/CHMP/ICH/135/1995)

Integrated Addendum - Key changes 1/5

Please refer to www.ich.org for full information

- GCP principles:
  - Applicability of GCP standards to all records, irrespective of the type of **media used**
  - Systems that assure quality should **focus** on the aspects of the trial that are **essential** to human subject protection and reliability of trial results

Integrated Addendum - Key changes 2/5

Investigator responsibilities

- **Supervise** individuals or parties to whom trial-related duties and functions are delegated (section 4.2.5)
- Ensure individuals and parties are qualified and **implement procedures** to ensure integrity of study tasks and data (4.2.6)
- Maintain adequate and accurate source documents and trial records (4.9.0). Source data should be attributable, legible, contemporaneous, original, accurate, and complete **(ALCOAC)**

Integrated Addendum - Key changes 3/5

Sponsor responsibilities

- Quality Management (section 5.0).
- Implement a system to manage quality throughout **all stages** of the trial process.
- Focus on trial activities **essential** to ensuring human subject protection and the reliability of trial results.
- Use methods to **assure and control** the quality of the trial that are proportionate to the risks.
- **Avoid** unnecessary complexity, procedures, and data collection

Integrated Addendum - Key changes 4/5

- Use a risk-based approach to the quality management system.
  - **Identify** critical processes and data (section 5.0.1)
  - **Identify** risks to critical trial processes and data (5.0.2)
  - **Evaluate** risks (5.0.3)
  - **Control** risks (5.0.4)
  - **Communicate** risks (5.0.5)
  - **Review** risks (5.0.6)
  - **Report** risks (5.0.7)

Integrated Addendum - Key changes 5/5

Sponsor responsibilities continued..

- **Oversight** of contract organisations (5.2.2)
- Computerised systems: validation based on **risk assessment** (5.5.3)
- Non compliance: requirement to perform **root cause analysis** and implement **corrective and preventative actions** (5.20.1)
- Monitoring (5.18.3):
  - risk based monitoring with **variety of approaches** possible
  - may include centralised monitoring of cumulative data
- Essential documents (8.1): **location(s)** of respective source documents to be recorded etc.

Current Status

- Date for coming into effect: 14 June 2017 (EMA/CHMP/ICH/135/1995)

- S.I 374 of 2006, Part 2, Regulation 17: *'The investigator and sponsor shall consider all relevant guidance with respect to commencing and conducting a clinical trial.'*

- Expectation: training of relevant personnel and implementation of requirements, as appropriate

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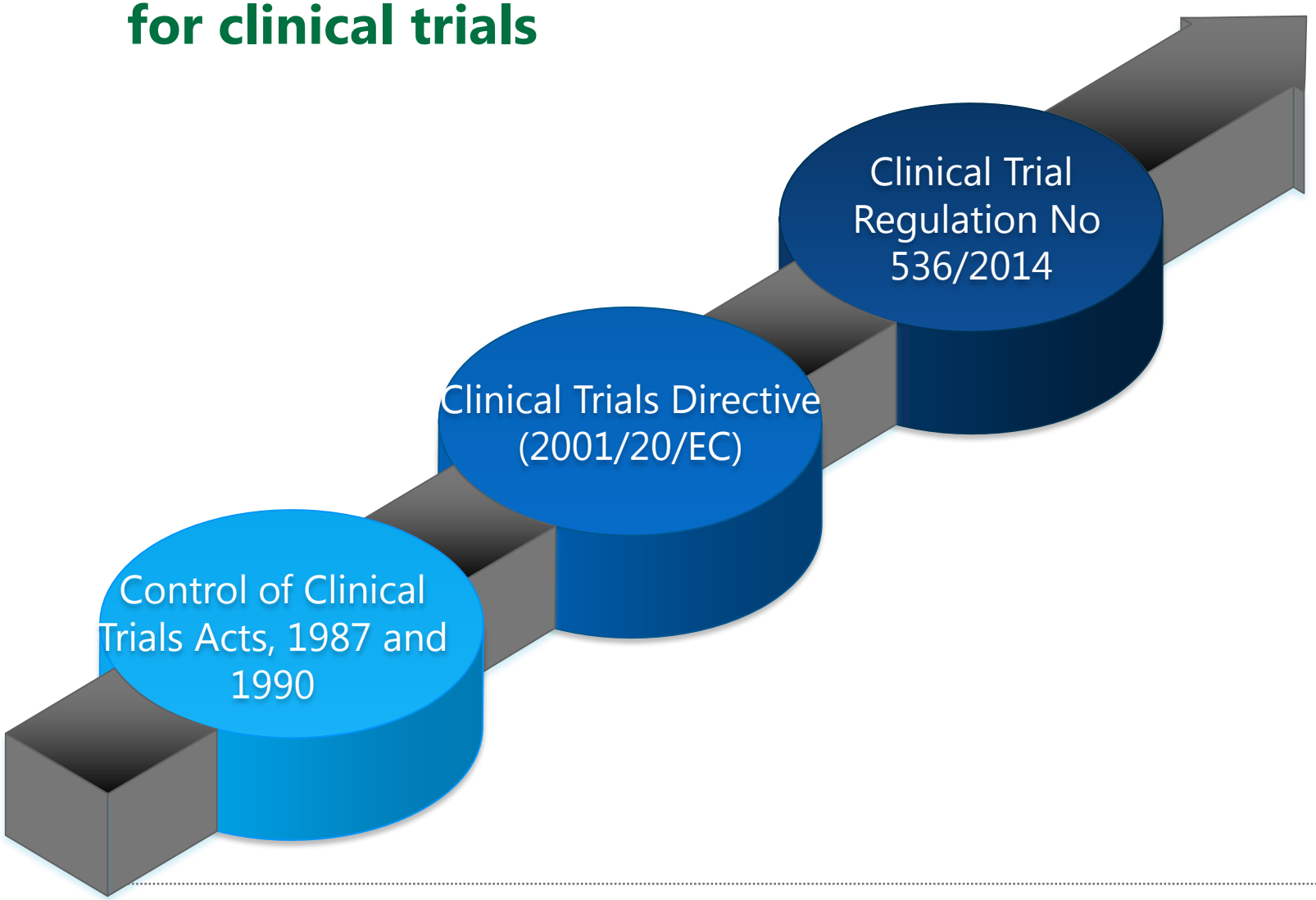
Clinical Trial Regulation No. 536/2014

Changes in regulatory environment for clinical trials



Background/objective

- CT Regulation will be directly applicable in all Member States
- Represents a major legislative change in the way clinical trials are conducted in EU
- Objectives;
  - To protect the rights, safety, dignity and well-being of subjects and the reliability and robustness of data generated in the CT
  - To foster innovation and simplify the clinical trial application process, in particular for multistate trials
  - To increase transparency, keeping the balance between protection of public health and fostering innovation capacity of European medical research while recognising the legitimate economic interests of sponsors
- Overall aim – Make EU attractive for R&D

New CT Regulation – Key changes 1/3

- **Single e-submission** via an EU portal (accessible to MS NCAs and Ethics Committees)
- **Harmonised dossier** (Annex I to the Regulation / language of the documents decided by each MSC)
- **Coordinated assessment** between Reporting MS and MS Concerned
- **One single decision** per Member State Concerned

New CT Regulation – Key changes 2/3

- Introducing a **risk adapted approach**:
  - Concept of low interventional trial (e.g. where IMP already authorised)
  - Providing for risk adapted approaches to activities including quality management, safety reporting, IMP management, trial management/monitoring and content of the Trial Master File
- **Simplifying safety reporting** requirements
- Introducing **mandatory reporting of serious breaches**
- **Increasing transparency** as regards clinical trials and their outcomes (protocol, results, inspections), whilst respecting data protection rules

New CT Regulation – Key changes 3/3

- **Informed consent - new provisions** for:
  - Broad consent (use of data outside the protocol)
  - For trial in minors and incapacitated subjects
  - For trials on pregnant and breastfeeding women
  - Member States to maintain measures for other vulnerable groups (e.g. persons in military service, deprived of liberty)
- Additional detail for conducting trials in the **emergency setting**
- Concept of **Co-sponsorship** introduced
- **Damage compensation system** to be set up by the Member States
- **Archiving** of the Trial master File – 25 years

Implementation and Transition Period

- Application:
  - Regulation adopted in 2014
  - Timing of application dependent on confirmation of full functionality of EU portal and database
  - Regulation will apply 6 months after publication of confirmation by European Commission
  - Expected second half of 2019

Implementation and Transition Period

- Transition:
  - 3 year period starting when Regulation becomes applicable
  - Year 1: CT can be submitted under old (Dir.) or new (Reg.) systems
  - Year 2&3: trials authorised under old system remain under that system
  - End of legacy: all CTs to switch to new Regulation 3 years after implementation

Further information

- Risk proportionate approaches in clinical trials – Recommendations of the expert group on clinical trials for the implementation of Regulation No 536/2014 on clinical trials of medicinal products for human use (25 April 2017) - https://ec.europa.eu/health/documents/eudralex/vol-10_en

- European Medicines Agency – Clinical Trial Regulation http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000629.jsp

- HPRA Clinical Trials page - http://www.hpra.ie/homepage/medicines/regulatory-information/clinical-trials

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Thank you