

# Addendum to ICH E6 (R2)

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for Pharmaceuticals for Human Use

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## Outline

1. Background
2. Addendum Objective
3. Addendum Format and Content
4. Implementation and Timelines

## 1. Background

## Statement of the perceived problem— why do we need an addendum to ICH E6?

- **Since 1996 adoption of ICH E6 GCP, clinical trials have evolved substantially;**
- **Increases in globalisation, study complexity, and technological capabilities;**
- **Approach to GCP needs modernisation to keep pace with the scale and complexity of clinical trials and to ensure appropriate use of technology.**

## Statement of the perceived problem— why do we need an addendum to ICH E6?

- **ICH E6 gave sponsors flexibility to implement innovative approaches – but has been misinterpreted and implemented in ways that impede innovation**
  - e.g. emphasising less important aspects of trials (e.g., focusing on the completeness and accuracy of every piece of data) at the expense of critical aspects (e.g., carefully managing risks to the integrity of key outcome data).
- **Modernising ICH E6 by supplementing it with additional recommendations will better facilitate broad and consistent international implementation of new methodologies.**

## 2. Addendum Objective

## Addendum to ICH E6 - Objective

- **This guideline has been amended to encourage implementation of improved and more efficient approaches to clinical trial design, conduct, oversight, recording, and reporting while continuing to ensure human subject protection and data integrity.**

## Harmonisation of Standards

### The current ICH E6 Expert Working Group includes:

- 14 representatives from the six ICH founding members (4 from US, 4 from EMA/EU, 6 from Japan)
- 2 experts/ one each from the two new ICH members Canada and Switzerland (Health Canada and Swissmedic joined the ICH Steering Committee in June 2014)
- 4 observers/one each from ANVISA (DRA of Brazil), DoH of Chinese Taipei, MFDS (DRA of Korea) and WSMI

## 3. Addendum Format and Content

## Addendum-Integrated Format

- (d) The review and follow-up of the monitoring report with the sponsor should be documented by the sponsor's designated representative.

### ADDENDUM

- (e) Monitoring results should be provided to the sponsor (including appropriate management and staff responsible for trial and site oversight) in a timely manner for review and follow up as indicated. Results of monitoring activities should be documented in sufficient detail to allow verification of compliance with the monitoring plan.

### ADDENDUM

#### 5.18.7 *Monitoring Plan*

The sponsor should develop a monitoring plan that is tailored to the specific human subject protection and data integrity risks of the trial. The plan should describe the monitoring strategy, the monitoring responsibilities of all the parties involved, the various monitoring methods to be used and the rationale for their use. The plan

## Addendum Content

- Introduction
- Glossary
  - certified copy,
  - monitoring plan,
  - monitoring report,
  - validation of computerized systems
- GCP Principles
  - applicability of GCP standards when using electronic media

## Addendum Content

- Investigator responsibilities:
  - Supervision of tasks delegated
  - Ensure qualification and implement procedures to ensure integrity
  - Source documents and trial records for each trial subject
    - Attributable, legible, contemporaneous, original, accurate, and complete

## Addendum Content

- Sponsor responsibilities
  - Quality Management
    - Sponsor should implement a system to manage quality throughout the design, conduct, recording, evaluation, reporting, and archiving of clinical trials
    - Sponsors should focus on essential trial activities
    - Methods used to assure and control quality of trial should be proportionate to risks
    - Avoid unnecessary complexity, procedures and data collected

## Addendum Content

- Sponsor responsibilities
  - Quality Management
    - risk-based approach to quality management,
      - Critical process & data identification
      - Risk Identification
      - Risk Evaluation
      - Risk Control
      - Risk Communication
      - Risk Review
      - Risk Reporting

## Addendum Content

- Sponsor responsibilities
  - oversight,
  - subcontracting by contract research organizations (CROs),
  - use of computerized systems,
  - follow-up of non-compliance



## Addendum Content

- Sponsor responsibilities
  - Monitoring- including risk based, centralised and on-site monitoring approaches,
    - Sponsor should develop a systematic, prioritised, risk-based approach
    - Permission of varied approaches e.g combination of on-site and centralised monitoring to improve effectiveness & efficiency
    - Rationale for chosen strategy should be documented
    - Documentation of monitoring results
    - Sponsor should develop monitoring plan tailored to the human subject protection and data integrity risks of the trial

17

## Addendum Content

- Essential Documents/(e)TMF
  - Sponsor and investigator should maintain record of location(s) of their respective essential documents. Storage system should provide for document identification, search and retrieval
  - Individual trials may require additional documents not mentioned in essential document list. Sponsor and/or investigator should include these as part of Trial Master File (TMF)
  - Investigator/institution should have control of all essential documents and records generated by the investigator/institution before, during and after the trial
  - When copy used to replace original document, it should fulfil requirements for certified copies

18

## Addendum Content

- Sponsor should not have exclusive control of Case Report Form (CRF) data
  - Sponsor should ensure that investigator has control of and access to CRF data reported to sponsor

## 4. Implementation and Timelines

## Implementation

- o This ICH GCP Guideline integrated Addendum provides a unified standard for the European Union (EU), Japan, the United States, Canada and Switzerland to facilitate the mutual acceptance of clinical data by the regulatory authorities in these jurisdictions.

## Workplan Timelines for Expert Working Group

Date	Task / Activity	Details
June/2015	Face to face meeting	<ul style="list-style-type: none"> <li>➤ Agreed on the addendum language and reached Step 1 draft</li> <li>➤ Updated the work plan</li> </ul>
July or August/2015 -Jan/2016	Public consultation by ICH and regional regulators	<ul style="list-style-type: none"> <li>➤ Gathering comments for review</li> </ul>
Feb/2016 -May/2016	Webconferences (5)	<ul style="list-style-type: none"> <li>➤ Reviewing and resolving comments received from public consultation and draft final document</li> </ul>
Jun/2016	Face to face meeting	<ul style="list-style-type: none"> <li>➤ Prepare final document</li> </ul>

ICH E6: Integrated Addendum: Good Clinical Practice



**Thank You!**

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