



Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2)

Prepared by the ICH E6(R2) Expert Working Group

February 2017

International Council for Harmonisation of Technical Requirements
for Pharmaceuticals for Human Use



ICH E6(R2) Addendum

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Outline

- Background
- Objective
- Format and Content
- Implementation

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 Good Clinical Practice (GCP) needs modernisation to keep pace with the scale and complexity of clinical trials and to ensure appropriate use of technology.

Background (continued): 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.
 - For example, emphasising less important aspects of trials (such as focusing on the completeness and accuracy of every piece of data) at the expense of critical aspects (such as 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.

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ICH E6(R2) - Objective

ICH E6(R1) 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 reliability of trial results.

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Integrated Format of the Addendum

- The addendum supplements ICH E6(R1) with additional text.
- This guideline should be read in conjunction with other ICH guidelines relevant to clinical trial conduct (for example, ICH E2A, E3, E7, E8, E9, and E11).
- In the event of any conflict between E6(R1) text and the addendum text, the addendum text should take priority.

Example of the Integrated Format of the Addendum

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

ADDENDUM

- (e) Reports of on-site and/or centralized monitoring 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. Results of monitoring activities should be documented in sufficient detail to allow verification of compliance with the monitoring plan. Reporting of centralized monitoring activities should be regular and may be independent from site visits.

Overview of Addendum Content

Introduction

Glossary

- Certified copy (section 1.63)
- Monitoring plan (1.64)
- Validation of computerized systems (1.65)

GCP Principles

- Applicability of GCP standards to all records, irrespective of the type of media used (section 2.10)
- Systems that assure quality should focus on the aspects of the trial that are essential to human subject protection and reliability of trial results (2.13)

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Overview of Addendum Content (continued)

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.

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Overview of Addendum Content (continued)

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.

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Overview of Addendum Content (continued)

Sponsor Responsibilities (continued)

- Quality Management (continued)
 - 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)

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Overview of Addendum Content (continued)

Sponsor Responsibilities (continued)

- Oversee trial-related duties and functions, including those that are subcontracted by Contract Research Organizations (CROs) (section 5.2.2).
- When using computerized systems, base the validation approach on a risk assessment, maintain standard operating procedures, and ensure data integrity (5.5.3(a) and 5.5.3(h)).
- Follow-up of non-compliance that has or may significantly affect human subject protection or reliability of trial results, by performing a root cause analysis and implementing corrective and preventive actions (5.20.1).

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Overview of Addendum Content (continued)

Sponsor Responsibilities (continued)

- Monitoring (sections 5.18.3, 5.18.6(e), and 5.18.7)
 - Develop a systematic, prioritised, risk-based approach.
 - Develop a monitoring plan tailored to the human subject protection and data integrity risks of the trial.
 - May use varied approaches to monitoring (for example, combination of on-site and centralized monitoring) to improve effectiveness and efficiency.
 - Document the rationale for the monitoring strategy.
 - Document results of monitoring activities.

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Overview of Addendum Content (continued)

Essential Documents (section 8.1)

- Sponsor and investigator should maintain a record of the location(s) of their respective essential documents. Storage system should provide for document identification, version history, search, and retrieval.
- Essential documents for a specific trial should be supplemented or may be reduced as appropriate.
- Sponsor should ensure that the investigator has control of and continuous access to the case report form data.

Overview of Addendum Content (continued)

Essential Documents (continued)

- When a copy is used to replace an original document, it should fulfill the requirements for certified copies.
- Investigator should have control of all essential documents and records generated by the investigator before, during, and after the trial.

Implementation

This ICH GCP Guideline Integrated Addendum provides a unified standard for the European Union, Japan, the United States, Canada, and Switzerland to facilitate the mutual acceptance of data from clinical trials by the regulatory authorities in these jurisdictions.

Thank You!