Addendum to ICH E6 (R2)

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AIFA

Dichiarazione di trasparenza/interessi*

Le opinioni espresse in questa presentazione sono personali e non impegnano in alcun modo l'AIFA

Interessi nell'industria farmaceutica	NO	Attualmente	Da 0 a 3 anni precedenti	oltre 3 anni precedenti
INTERESSI DIRETTI:				
1.1 Impiego per una società: Ruolo esecutivo in una società farmaceutica	☒	☐	☐	☐ obbligatorio
1.2 Impiego per una società: Ruolo guida nello sviluppo di un prodotto farmaceutico	☒	☐	☐	☐ obbligatorio
1.3 Impiego per una società: altre attività	☒	☐	☐	☐ facoltativo
2. Consulenza per una società	☒	☐	☐	☐ facoltativo
3. Consulente strategico per una società	☒	☐	☐	☐ facoltativo
4. Interessi finanziari	☒	☐	☐	☐ facoltativo
5. Titolarità di un brevetto	☒	☐	☐	☐ facoltativo
INTERESSI INDIRETTI:				
6. Sperimentatore principale	☒	☐	☐	☐ facoltativo
7. Sperimentatore	☒	☐	☐	☐ facoltativo
8. Sovvenzioni o altri fondi finanziari	☒	☐	☐	☐ facoltativo
9. Interessi Familiari	☒	☐	☐	☐ facoltativo

* Angela Del Vecchio, secondo il regolamento sul Conflitto di Interessi approvato dal CdA AIFA in data 25.03.2015 e pubblicato sulla Gazzetta Ufficiale del 15.05.2015 in accordo con la policy EMA /626261/2014 sulla gestione del conflitto di interessi dei membri dei Comitati Scientifici e degli esperti.

N.B. Il compenso ricevuto per questo intervento è regolato dalla contrattazione collettiva

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Agenda

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

Background

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

Background

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 <u>better facilitate</u> broad and consistent international implementation of new methodologies

Harmonisation of Standards

ICH E6 Expert Working Group composition:

- ✓ 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

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.

What is an addendum?

- A new text, of equal regulatory value to the original text.
- It does not replace the original text but adds to it.
- Novel approach for ICH introduced with the GCP addendum- the new text is inserted in the right places next to the original text, rather than as a separate document that would have been confusing.

Addendum-Integrated Format

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

5.18.6 Monitoring Report

(a) The monitor should submit a written report to the sponsor after each trial-site visit or trial-related communication.

(b) Reports should include the date, site, name of the monitor, and name of the investigator or other individual(s) contacted.

(c) Reports should include a summary of what the monitor reviewed and the monitor's statements concerning the significant findings/facts, deviations and deficiencies, conclusions, actions taken or to be taken and/or actions recommended to secure compliance.

(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.

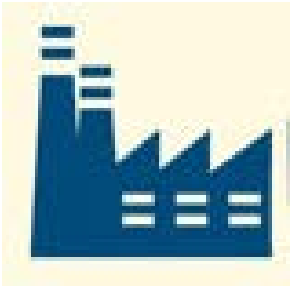
Addendum Content

- 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 subject
    - attributable,
    - legible,
    - contemporaneous,
    - original,
    - accurate, and complete

Addendum Content



- Sponsor responsibilities
  - ✓ Quality Management
    - implement a system to manage quality throughout the design, conduct, recording, evaluation, reporting, and archiving of clinical trials
    - 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
  - ✓use of computerized systems
  - ✓follow-up of non-compliance

Addendum Content

- Sponsor responsibilities
  - ✓ Monitoring - including risk based, centralised and on-site
    - 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

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

Addendum Content

- Sponsor should not have exclusive control of Case Report Form (CRF) data

should ensure that Investigator has control of and access to CRF data reported to sponsor

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE (ICH)

ICH HARMONISED GUIDELINE

INTEGRATED ADDENDUM TO ICH E6(R1): GUIDELINE FOR GOOD CLINICAL PRACTICE

E6(R2)

Current *Step 4* version

dated 9 November 2016

Grazie dell'attenzione !!!

CONTATTI

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