AGENZIA ITALIANA DEL FARMACO

Tutela Ricerca e Sviluppo per la Salute

Addendum to ICH E6(R2)

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24/05/2019

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	X	☐	☐	☐ obbligatorio
1.2 Impiego per una società: Ruolo guida nello sviluppo di un prodotto farmaceutico	X	☐	☐	☐ obbligatorio
1.3 Impiego per una società: altre attività	X	☐	☐	☐ facoltativo
2. Consulenza per una società	X	☐	☐	☐ facoltativo
3. Consulente strategico per una società	X	☐	☐	☐ facoltativo
4. Interessi finanziari	X	☐	☐	☐ facoltativo
5. Titolarità di un brevetto	X	☐	☐	☐ facoltativo
INTERESSI INDIRETTI:				
6. Sperimentatore principale	X	☐	☐	☐ facoltativo
7. Sperimentatore	X	☐	☐	☐ facoltativo
8. Sovvenzioni o altri fondi finanziari	X	☐	☐	☐ facoltativo
9. Interessi Familiari	X	☐	☐	☐ 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. <Per questo intervento non ricevo alcun compenso>

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 for study and new molecules complexity, and technological capabilities
- The consequences of this complex process has led to the transferring of trial-related duties of the Research process to the third-parties.
- This outsourcing raised questions as the sponsor can monitor the process of a clinical trial and ensure data integrity when using a computerized system in a clinical trial

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
- Approach to GCP needs modernisation to take into account the complexity of clinical trials and to ensure appropriate use of technology
- Many GCP inspection reports around the world listed critical findings related to the CSR, data management and inadequacy of monitoring activities, that demonstrate an inadequate QC and decreased sponsor oversight.

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
- ✓ 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.

Addendum to ICH E6 - Objective

- The 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 authorithies in these jurisdictions.
- In the event of any conflict between E6 (R1) text and the E6 (R2) addendum text, the E6 (R2) addendum text should take priority.

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

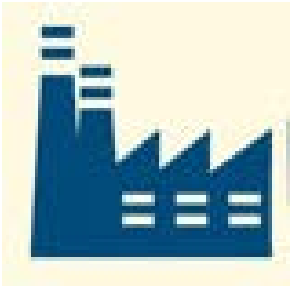
- Glossary
  - certified copy
  - monitoring plan
  - validation of computerized systems

- GCP Principles
  - applicability of GCP standards when using electronic media
  - systems that assure quality should focus on the aspects of the trial that are essential to human subject protection and reliability of results

Addendum Content

- Investigator responsibilities:
  - ✓ Supervision of tasks delegated
  - ✓ Ensure qualification and implement procedures to ensure integrity of study tasks an data
  - ✓ 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 collection

Addendum Content

- Sponsor responsibilities
  - ✓Quality Management should use a risk-based approach
    - Critical process & data identification
    - Risk Identification
    - Risk Evaluation
    - Risk Control
    - Risk Communication
    - Risk Review
    - Risk Reporting

Addendum Content

- Sponsor responsibilities

  - ✓Oversight of any duty or function carried out on its behalf subcontracted to Contract Research Organizations

  - ✓use computerized systems with a validation approach based on a risk assessment

  - ✓follow-up of significant non-compliance by performing a root cause analysis and implementing CAPA

Addendum Content

- Sponsor responsibilities
  - ✓Monitoring
    - 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 and 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
  - Sponsor and investigator should maintain record of location(s) of their respective essential documents. Storage system should provide for document identification, search and retrieval.
  - Essential documents should be supplemented or may be reduced
  - Investigator should have control of all essential documents and records generated by the investigator before, during and after the trial

Addendum Content

- When copy used to replace original document it should fulfil requirements for certified copies

- 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

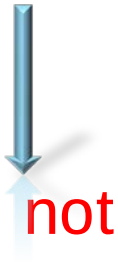
E6(R2)

Current *Step 4* version

dated 9 November 2016

Conclusion

- The new GCP represents the biggest revision of the international ICH GCP guidelines for over 20 years and has the potentional to alter the way in which clinical research is managed.
- It is clear the need to modernise GCP
- Risk based approaches are well defined
- New tools and approaches are indicated
- Greater use of electronically data
- Many facilitations for CTs using new approaches



GCP is a tool not an obstacle

Grazie per l'Attenzione!

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