Addendum to ICH E6

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1. Why ICH-E6 should be revised?
2. How is ICH-E6 changing?
3. Points of ICH-E6 addendum
   a. Quality management
   b. Clinical trial monitoring
   c. Electronic records
   d. Essential documents
   e. Others
ICH-E6 is...

ICH-E6 -GUIDELINE FOR GOOD CLINICAL PRACTICE-

✓ Reached consensus on final guideline (Step 4) in 1996, as an international *ethical and scientific* standard for clinical trials based on Declaration of Helsinki.

✓ To facilitate the mutual acceptance of clinical data. (Compliance with ICH-E6 is necessary for acceptance of the data by EU, US and Japan.)

✓ Japan implemented ICH-E6 into the regulation in 1997.
Why do we need an addendum to ICH E6?

Since 1996 adoption of ICH E6, clinical trials have evolved substantially.

- Increase of site & scale of development, also the cost!
- Change in approach to quality (risk) management (new concepts for quality of clinical trials)
- Evolution in technology (mainly in IT area which leads utilization of electronic records)
- Subdivision & complication of tasks (internal assignment, outsourcing)

Approach to GCP needs modernization
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### Work plan for ICH-E6(R2) EWG

<table>
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<th>Timeline</th>
<th>CONTENTS</th>
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<tr>
<td>Nov/2013</td>
<td>US-FDA proposed “Assessment of Clinical Trial Quality” as a new topic in ICH Osaka meeting</td>
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<tr>
<td>Apr/2014</td>
<td>Steering Committee approved the draft Concept Paper</td>
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<tr>
<td>Jun/2014</td>
<td>E6 (R2) EWG meeting in ICH Minneapolis (First Face-to-Face meeting)</td>
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<td>Jul~Nov/2014</td>
<td>Web conference (6 times) &amp; EWG F2F in ICH Lisbon</td>
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<tr>
<td>Feb~Jun/2015</td>
<td>WC (x 6) &amp; EWG F2F in ICH Fukuoka</td>
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<tr>
<td>Jul/2015</td>
<td>Step 2b Draft Guideline</td>
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<tr>
<td>~Jan/2016</td>
<td>Public consultation</td>
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<tr>
<td>Feb-Jun/2016</td>
<td>WC (x 5) &amp; EWG F2F in ICH Lisbon, Step 3 sign off</td>
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<tr>
<td>Nov/2016</td>
<td>Step 4 sign off in ICH Osaka</td>
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Revision policy

No change in the original text of ICH-E6, and providing addendum.

* In the event of any conflict between the E6(R1) text and the E6(R2) addendum text, the E6(R2) addendum text should take priority

Objective

✓ 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
(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
Scope of the addendum

Scope of ICH-E6(R2) Expert Working Group

• To facilitate innovative approaches to GCP to better ensure data quality and human subject protection
  – Quality management
  – Clinical trial monitoring
  – Electronic records
  – Essential documents
# Summary of addendum content 1

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<td>Introduction</td>
<td>Background</td>
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| 1. GLOSSARY            | 1.63 Certified Copy  
1.64 Monitoring Plan  
1.65 Validation of computerized systems                                                                 |
| 2. PRINCIPLES          | 2.10 Data handling, etc. (to apply the item to all media type)  
2.13 Quality assurance (to focus on essential matters)                                                                 |
| 4. INVESTIGATOR        | 4.2.5 Supervision of delegated tasks  
4.2.6 Ensure qualification of staffs and implement procedures to ensure integrity  
4.9.0 Source documents and trial records for each trial subject (ALCOA) |
## Summary of addendum content 2

<table>
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<th>Section</th>
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<td>5. SPONSOR</td>
<td>5.0 Quality management</td>
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<td></td>
<td>5.2.2 Oversight of subcontracted tasks by CRO</td>
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<td>5.5.3 Use of computerized systems (Validation, SOP, data integrity)</td>
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<td>5.18.3 Extent and nature of monitoring (Risk-based monitoring, Centralized monitoring)</td>
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<td>5.18.7 Monitoring plan</td>
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<td>5.20.1 Non compliance</td>
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<td>8. Essential Documents</td>
<td>8.1 (Documents handling)</td>
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Agenda

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(Points) a. Quality management

Concept (for efficiency)
Limited resources should be used to where it is really necessary.

High risk part.

- For subject protection
- For reliability of trial results

(=For protection of future patients)

Risk-based approach!

= Sections 2.13, 5.0 (, 5.20.1)

(Ref. next presentation)
Recommending introducing...

- Risk-based monitoring
- Centralized monitoring

✓ Monitoring is one of quality management (QM) activities.
  ➡️ Also should be risk-based.

✓ Centralized monitoring will improve quality & QM.
  ➡️ Utilization of IT (internet, electronic records) make it possible.

= Section 5.18.3 (, 5.18.6(e), 5.18.7, 1.64)

(Ref. next presentation)
Electronic records should be handled considering below.

✓ Need validation if the system has essential function.
  = Sections 1.65, 5.5.3(a)

✓ Need SOP.
  = Section 5.5.3(b)

✓ Points for Data reliability & Certified copy
  (Not only for electronic records)
  = Section 1.63, 2.10, 4.9.0, 5.5.3(h), 8.1

(Ref. next presentation)
Section 8.1

✓ Introduced flexibility to supplement or reduce essential document list when justified
✓ Appropriate maintenance (record of location, storage/archiving, certified copy)
✓ Investigators should have control of their documents, especially for source data/documents.
Oversight of contracted individuals/parties tasks

- Investigator responsibilities
  - = Sections 4.2.5, 4.2.6
- Sponsor responsibilities
  - = Section 5.2.2
Thank you for your attention!!

太谢谢了
ご清聴ありがとうございました

International Collaboration (Win-Win Relationship)

2016 Conference on Good Clinical Practice