

Final Business Plan
Addendum for ICH E6: Guideline for Good Clinical Practice
dated 4 June 2014

Endorsed by the ICH Steering Committee on 5 June 2014

1. The issue and its costs

- *What problem/issue is the proposal expected to tackle?*

Since the adoption of the ICH E6 Guideline on *Good Clinical Practice (GCP)*, clinical trials have evolved substantially, with increases in globalisation, study complexity, and technological capabilities. To keep pace with the scale and complexity of clinical trials and to ensure appropriate use of technology we propose to modernise our approach to GCP to enable implementation of innovative approaches to clinical trial design, management, oversight, conduct, documentation, and reporting that will better ensure human subject protection and data quality. Although ICH E6 generally can be interpreted as providing sponsors flexibility to implement innovative approaches, it has been misinterpreted and implemented in ways that impede innovation by, for example, 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).

- *What are the costs (social/health and financial) to our stakeholders associated with the current situation or associated with “non action”?*

FDA, EMA, and MHLW/PMDA have recently issued documents related to clinical trial quality. FDA's guidance focuses on a portion of quality management, risk-based approaches to clinical trial oversight by sponsors. EMA's reflection paper is broader in scope and discusses risk-based quality management in clinical trials. MHLW/PMDA's document provides the fundamental ideas of risk-based monitoring in clinical trials. Prioritised, proactive quality management approaches to clinical trials are supported by industry to ensure data quality and human subject protection. A harmonised guideline on approaches to quality management for clinical trials could improve the protection of trial participants and the reliability of trial results. Lack of harmonisation may not only slow the adoption of innovative approaches to clinical trial design, management, oversight, conduct, documentation, and reporting, but may also lead to inconsistency in approaches sponsors use among the ICH regions which could add cost and time to the development of needed drug products.

2. Planning

- *What are the main deliverables?*

It is proposed that ICH develop an addendum to supplement ICH E6 with recommendations to facilitate innovative approaches to clinical trials including quality risk management and quality-by-design processes which emphasise upfront assessment of risks specific to a study design and protocol. Study operational procedures to facilitate innovative approaches should be addressed, including risk-based monitoring, focusing on critical study elements, and use of technological tools to ensure robust conduct, oversight, and reporting.

- *What resources (financial and human) would be required?*

An Expert Working Group (EWG) should be established. The EWG should include two members nominated by EU, EFPIA, FDA, PhRMA, MHLW, JPMA, Health Canada and Swissmedic. One member can also be nominated by WHO Observer, WSMI, IGPA, biotech industry as well as RHIs, DRAs/DoH (if requested). Members should include experts in good clinical practice with experience in clinical trial quality management. EWG members' sponsoring organisations would need to provide financial resources for any needed face-to-face meetings (anticipate two or three face-to-face meetings).

- *What is the time frame of the project?*

Summer 2014 through mid 2017.

Most work will be conducted via teleconferences and email; a face-to-face meeting is planned for June 2014. Two additional face-to-face meetings may be needed. An 18-month interval is anticipated between the *Step 2* and *Step 4* documents to allow the usual consultation.

What will be the key milestones?

The established ICH processes and procedures should be followed. It is expected that the work of the EWG will be completed within this general schedule:

Step 2 guideline: June 2015

Step 4 guideline: November 2016

3. **The impacts of the project**

- *What are the likely benefits (social, health and financial) to our key stakeholders of the fulfilment of the objective?*

Since many pharmaceutical companies conduct Multi-Regional Clinical Trials, harmonised recommendations on risk management and quality-by-design processes would improve the business efficiency of industry and would promote a focus on high value activities that may improve human subject protection and reliability of trial results.

- *What are the regulatory implications of the proposed work – is the topic feasible (implementable) from a regulatory standpoint?*

Some ICH Parties have recently issued documents related to clinical trial quality, though the scope of the documents is different. The topic is feasible from a regulatory standpoint.

4. **Post-hoc evaluation**

- *How and when will the results of the work be evaluated?*

The results will be evaluated by:

- Implementation of local regulations and/or guidance documents that align with the final guideline;
- *Ad hoc* feedback from stakeholders.