Final Concept Paper
Addendum for ICH E6: Guideline for Good Clinical Practice
dated 2 June 2014
Endorsed by the ICH Steering Committee on 5 June 2014

Type of Harmonization Action Proposed

Addition of an addendum to an existing Guideline, ICH E6, *Good Clinical Practice (GCP)*: Consolidated Guideline

Statement of the Perceived Problem

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 should 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). Modernising ICH E6 by supplementing it with additional recommendations will better facilitate broad and consistent international implementation of new methodologies. Topics to be discussed by the expert working group (EWG) to facilitate innovative approaches to clinical trials include quality risk management and quality-by-design processes which emphasizs upfront assessment of risks specific to a study design and protocol. In addition, other study operational procedures to facilitate innovative approaches should be discussed, including risk-based monitoring, focusing on critical study elements, and use of technological tools to ensure robust conduct, oversight, and reporting.

Issues to be Resolved

ICH E6 should be supplemented with additional recommendations to facilitate innovative approaches to GCP to better ensure data quality and human subject protection in an environment of highly complex multinational trials.

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. ICH has issued guidelines on pharmaceutical quality systems and quality risk management that are critical to advancing global manufacturing standards. A harmonised guideline on approaches to quality management for clinical trials, including risk-based monitoring and supporting the use of new technology could have a similar impact on the protection of trial participants and the

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reliability of trial results. Prioritised, proactive quality management approaches to clinical trials are supported by industry to ensure data quality and human subject protection.

Background to the Proposal

- ICH E6, *Good Clinical Practice*: Consolidated Guideline
- US FDA, Guidance for Industry Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring, 2012
- EMA, Reflection Paper on Risk Based Quality Management in Clinical Trials, 2013
- MHLW, Fundamental Notion on Risk Based Monitoring in Clinical Trials, 2013
- ICH Q9, Quality Risk Management
- Clinical Trials Transformation Initiative workshops on quality by design and quality risk management
- TransCelerate Biopharma, Inc. risk-based monitoring resources
- Sensible Guidelines for the Conduct of Clinical Trials meetings, 2007-2012

Type of Expert Working Group and Resources

The EWG will be comprised of 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).

Timing

Work should be conducted primarily by email and teleconferences. Two or three face to face meetings may be necessary to address difficult topics.