

Final Concept Paper
E17: General principle on planning/designing Multi-Regional Clinical Trials
dated 21 May 2014
Endorsed by the ICH Steering Committee on 5 June 2014

Type of Harmonisation Action Proposed

This Concept Paper supports a proposal for a new harmonised tripartite guideline on general principles on planning/designing Multi-Regional Clinical Trial (MRCT).

Statement of the Perceived Problem

Drug development has rapidly been globalized recently and MRCT for regulatory submission has widely been conducted in non-ICH regions as well as ICH regions. Regulatory agencies currently face challenges in evaluating data from MRCTs for drug approval. However, there is currently no harmonised ICH Guideline on MRCTs, especially focusing on scientific issues in planning/designing MRCTs, although Q&A of ICH E5 Guideline partly covers issue relating to MRCTs. An international guideline will be needed to promote conducting MRCT appropriately. A lack of harmonisation on this topic may cause additional burden for sponsor and difficult situation for conducting MRCTs.

Issues to be Resolved

The new guideline will describe practical issues in planning/designing MRCT. Issues on data interpretation may be discussed in a process of discussion for establishing this guideline, but are out of scope in this guideline. Main objective of this guideline is to provide common points to consider in planning/designing MRCTs and minimize conflicting opinions from regulatory bodies. The below may be examples of topics covered in this guideline, but more details will be determined by discussion among experts of the group.

- Issues in planning MRCTs
 - Usefulness of MRCTs in drug developments
 - Essential points for conducting MRCTs (GCP etc)
 - Importance of ethnic factors evaluation on drug efficacy/safety in MRCTs etc.
- Issues in designing MRCTs
 - Points to consider in dose determination for MRCT (exploratory and confirmatory)
 - How to control various concomitant medications in each country
 - Consideration on definition of a population and methods of sample size estimation for a population/region etc.
- Others
 - Encouraging a parallel scientific consultation with multiple regulatory agencies in advance

Background to the Proposal

In recent years, data from MRCTs have usually been submitted to multiple regulatory agencies in ICH and non-ICH regions. Guidelines and other related documents on this topic have been published in Japan and EU (Japan; Basic principles on global clinical trials, Notification No.0928010, September 28th, 2007, EU; Reflection paper on the extrapolation of results from clinical studies conducted outside of the EU to the EU population, EMEA/CHMP/EWP/692702/2008, October 22nd, 2009). US FDA also recently published their perspective regarding MRCTs (ref. Clin Pharmacol Ther 94: 230, 2013). International harmonisation on this topic will promote to conduct MRCTs more appropriately and increase an efficiency of drug development, resulting in avoiding duplicative works in drug development and a better regulatory decision.

Type of Expert Working Group and Resources

It is proposed that an ICH Expert Working Group (EWG) be established and mandated to draft an ICH guideline on general principles on planning/designing MRCTs. The EWG will consist of two or three members nominated by EU, EFPIA, FDA, PhRMA, MHLW, JPMA, Health Canada and Swissmedic. One member can also be nominated by WHO Observer, RHIs and DRAs/DoH (if requested).

Timing

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| • Approval of Concept Paper by Steering Committee | June 2014 |
| • Establishment of EWG | 2Q 2014 |
| • First face-to-face EWG Meeting | 4Q 2014 |
| • Discussion by e-mail, web-based conference or teleconference | 4Q 2014 - 3Q 2015 |
| • Second face-to-face EWG Meeting for adaption of <i>Step 2</i> document | 4Q 2015 |
| • Public consultation | 4Q 2015 - 2Q 2016 |
| • Revision of guideline based on comments received | 2Q 2016 - 3Q 2016 |
| • Third face-to-face EWG Meeting for adaption of <i>Step 4</i> document | 4Q 2016 - 1Q 2017 |