

Final Concept Paper
E18: Genomic Sampling and Management of Genomic Data
dated 5 March 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 ICH Guideline on general principles on *genomic sample collection in clinical trials and other studies for future use*.

Statement of the Perceived Problem

Genomic data have become important to evaluate efficacy and safety of a drug for regulatory approval. As a result, genomic information has been increasingly included in drug label relevant for the benefit/risk evaluation of a drug. To accumulate such data during drug development and throughout the product life cycle, genomic samples should be collected in clinical trials and other studies following a certain methodology and be stored for certain periods. It has been reported that collection rate of such samples is still low in many ICH regions (ref. Clin Pharmacol Ther 89: 529, 2011). All ICH regulatory agencies (EMA, FDA and MHLW/PMDA) have independently published guidelines encouraging genomic sample collection. Although ICH E15 Guideline describes definition of sample coding, there is currently no harmonised ICH Guideline on genomic samples collection in clinical trials or other studies.

Harmonisation across regions on this topic will maximize the information gathered from the studies for e.g., sample collection and analysis (including ethical considerations) and facilitate implementation of pharmacogenomics for the benefit of all stakeholders.

On the contrary, lack of harmonisation could delay such implementation affecting drug development, healthcare delivery with consequent impact on the sponsors, patients and public.

Issues to be Resolved

Harmonised guidance on *Genomic Sampling Methodologies for Future Use* will clarify points to consider in collecting Genomic samples in clinical trials and other studies and will reduce or obviate duplication of pharmacogenomic studies carried out during the research and development of new drugs. Storage of genomic samples and data in clinical studies may be subject to national laws and regulations. This guideline focuses on the technical aspects relating to collection, handling and storage of genomic samples for future use and supports robust methodology, investigators' activity and ethic committees' considerations.

The following issues have been identified from past practical experiences and will need to be addressed in this guideline:

- Situations, value and importance of appropriate methodology in planning Genomic sample collection for future use:
 - To enable retrospective analysis when new scientific evidence is emerges or when additional analysis of Genomic samples becomes necessary;

- To enable analysis/evaluation using sufficient number of samples obtained from multiple clinical trials.
- Recommendations for genomic sampling in clinical trials and other studies:
 - Genomic sample collection and handling: (1) Samples should be obtained without selection bias; (2) Appropriate use of coded samples and anonymised/anonymous samples (Coded samples would be utilised in investigation for confirmatory objectives, whose data will be submitted to regulatory authority; anonymised/anonymous samples and data, including clinical outcome and subject demographics, may be utilised in investigation for exploratory objectives) in accordance with ICH E15 Guideline including data handling;
 - Genomic sample storage, i.e. it is important to establish and keep the best conditions where the target analyte is stable regardless of specimen storage for appropriate evaluation.

Background to the Proposal

Majority of the drugs are now globally developed and genomic data associated with efficacy or safety have been submitted to multiple regulatory agencies in ICH and non-ICH regions. Genomic data are useful in evaluating differences or similarities of drug efficacy/safety between responder and non-responder or between high risk and low risk populations. Scientific discussion on *Genomic Sampling Methodologies for Future Use* has been published based on accumulated regulatory experiences (ref. Pharmacogenomics 14: 103, 2013, Nature Rev Drug Discov 12: 103, 2013). International harmonisation on this topic will further encourage the collection of genomic samples in a standardised way and facilitate the use of pharmacogenomics in drug development, resulting in promotion of better regulatory decision making to the benefit of the public and the patient.

To date, no comprehensive guideline describing the contents described under “**Issues to be Resolved**” exists in any ICH region. However, the following documents mention some of the related issues:

- **Japan:** Guideline on General Principles for Clinical Trials Using Pharmacogenomics (Notification No. 0930007, Evaluation and Licensing Division, MHLW, September 2008).
Technical Guidance on Development of In Vitro Companion Diagnostics and Corresponding Therapeutic Products (PMDA Notification No. 1224029, December 2013).
- **US:** Guidance for Industry Clinical Pharmacogenomics: Premarket Evaluation in Early-Phase Clinical Studies and Recommendations for Labeling (FDA, January 2013)
- **EU:** Reflection Paper on Pharmacogenomic Samples, Testing And Data Handling (Doc. Ref. EMEA/CHMP/PGxWP/201914/2006)

Referring to the documents mentioned above, a new guideline will integrate the experiences of both regulatory authorities and pharmaceutical industries. This guideline will provide recommendations through this process of prospective harmonisation. This guideline intends to establish harmonised *Genomic Sampling Methodologies for Future Use*, for enabling a more efficient global drug development.

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 *Genomic Sampling Methodologies for Future Use*. The EWG shall consist of two or three members (clinical experts) 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

- Approval of Concept Paper by Steering Committee June 5 2014
- First face-to-face EWG Meeting 4Q 2014
- Second face-to-face EWG Meeting for reaching *Step 1* document 2Q 2015
- Third face-to-face EWG Meeting for adoption of *Step 2* document 4Q 2015