Final Concept Paper
E15: Terminology in Pharmacogenomics
dated 5 April 2006
Endorsed by the ICH Steering Committee on 19 April 2006

Type of Harmonisation Action Proposed

A new harmonised ICH guideline on terminology for pharmacogenetics, pharmacogenomics, sample and data coding and genomic biomarkers.
Standardised terminology will be proposed for incorporation in future regulatory documents related to pharmacogenetics and pharmacogenomics.

Statement of the Perceived Problem

Harmonisation of terminology, definitions (and broad identification of associated implications) is a pre-requisite topic where timely harmonisation will create a common foundation upon which future pharmacogenetic and pharmacogenomic guidance and regulations can be built.
Inconsistent definitions currently make it difficult to achieve agreement on parameters for implementation of pharmacogenetics and pharmacogenomics in global pharmaceutical development, and might also lead to inconsistent assessments by regulators.

Issue to be resolved

The FDA, EMEA/CHMP and MHLW have already included definitions for pharmacogenetics and pharmacogenomics terminology in public presentations and published guidance documents. Examples include the definitions referring to coding (and implications thereof) of research samples and data described in the EMEA/CHMP Position Paper on Terminology in Pharmacogenetics[1] and the genomic biomarker definitions described in the FDA Guidance for Industry Pharmacogenomic Data Submission[2] in relation to validity of biomarkers. To date, however, none of the organisations has formally endorsed the others' definition and divergence in opinion may arise.

Background to the proposal

Reference documents compiled to date by ICH parties:

- EFPIA Pharmacogenetic Ad Hoc Group - Draft concept paper on the harmonisation of pharmacogenetic /pharmacogenomic terminology
- JPMA Pharmacogenomics Group of the Drug Evaluation Committee - Review of existing regulatory guidance documents available in the regions.
- JPMA - Points to consider for pharmacogenomics application in clinical trials
- Existing regulatory guidelines (FDA, EMEA, MHLW) of the participating Regions.

[1] CPMP Position Paper on Terminology in Pharmacogenetics [EMEA/CPMP/3070/01, November 2002]

[2] Guidance for Industry Pharmacogenomic Data Submissions. March 2005.
http://www.fda.gov/cder/guidance/index.htm

1.Definition of pharmacogenetics and pharmacogenomics

The terms pharmacogenetics and pharmacogenomics have been defined by the CHMP, FDA, MHLW[3] and the pharmaceutical industry Pharmacogenetics Working Group (PWG)[4]. The terms pharmacogenetics and pharmacogenomics have not yet been used in ICH guidance. The published definitions are inconsistent among these four groups and yet are often used interchangeably. This has implications for the scope (both in preclinical and clinical development) in which the respective guidance documents can be applied.

Proposed Topic Focus

- **Restrict definition scope to DNA variation and RNA expression**
- **Promote broad definition that has flexibility to adapt as scientific knowledge expands**
- **Identify any context and operational implications for the use of the definitions**

2.Sample and Data Coding Definition

There is a need for clear recommendations for sample and data coding procedures across the ICH Regions. How pharmacogenomic samples and data are coded has critical direct impact on the use of samples and data for R&D decisions and in regulatory assessment. For this reason, CHMP[2] and the industry Pharmacogenetics Working Group (PWG) [5] have published terminology and five categories referring to the coding and their implications. Neither the FDA nor MHLW have endorsed these definitions and some clarification is required.
There is no consistent recommendations across the Regions on how these data may be used in regulatory assessment.

Proposed Topic Focus

- **Define benefits and limitations of specific coding procedures**
- **Identify implications of coding procedure on e.g. sample storage, audit trails, regulatory assessment, post-approval follow-up**

3.Genomic Biomarker Definition

The FDA guidance on Pharmacogenomic Data Submission[3] introduced biomarker definitions to distinguish between biomarkers which may be appropriate for regulatory decision-making from those less well-developed that are still exploratory.
The CHMP draft Guidelines on Pharmacogenetics Briefing Meetings[6] uses the same definition of biomarker as that quoted in the FDA guidance, but refers specifically to pharmacogenetic biomarkers.

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[3] "Submission of Information to Administrative Bodies Regarding the Preparation of Guidelines on the Usage of Pharmacogenomics in Clinical Studies on Drugs". MHLW, Pharmaceutical and Food Safety Bureau, Evaluation and Licensing Division. 18 March 2005

[4] Anderson DC., Gomez-Mancilla B., Spear BB., Barnes DM., Cheeseman K., Shaw, PM., Friedman J., McCarthy A., Brazell C., Ray SC., McHale D., Hashimoto L, Sandbrink R., Watson M.L., Watson M.L., Salerno RA., Lister C. on behalf of the Pharmacogenetics Working Group (2002). Elements of informed consent for pharmacogenetic research: Perspective of the Pharmacogenetics Working Group. Pharmacogenomics Journal. 2: 284.

[5] Pharmacogenetics Working Group. (2001) Terminology for sample collection in clinical genetic studies. Pharmacogenomics Journal. 1: 101-103

[6] CPMP draft Guideline on the Pharmacogenetics Briefing Meetings [CPMP/20227/2004 March 17, 2005]

Early discussions on the definition of attributes of genomic biomarkers, would facilitate incorporation of pharmacogenomics in global drug development.

Proposed Topic Focus

- **Establish definitions for what variables constitute genomic biomarkers.**

Issues that will not be addressed in the proposed guideline include:

• processes of validation or qualification
• evidence to validate or qualify genomic biomarkers for their intended use
• criteria for mutual acceptance genomic markers across regions

TYPE OF EXPERT WORKING GROUP

It is proposed that an ICH Expert Working Group be established and mandated to draft an ICH guideline on pharmacogenomic terminology.