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2 EMA/CHMP/PGWP/415990/2014
3 Committee for Medicinal Products for Human Use (CHMP)

4 Concept paper on good genomics biomarker practices

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Agreed by Pharmacogenomics Working Party	April 2014
Adopted by CHMP for release for consultation	24 July 2014
Start of public consultation	4 August 2014
End of consultation (deadline for comments)	4 November 2014

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Keywords	***Genomics, biomarker, pharmacogenomics, clinical trials, methodologies, genomic analyses***

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1. Introduction

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 labels relevant for the benefit/risk evaluation of a drug and consequently as guidance for patient treatment.

The integration of genomic biomarkers in clinical trials and other studies, as well as the technology used, should follow certain principles considering the biomarkers' implications on the studies, their analyses and outcome, with the intention to maximise the benefit for patient treatment.

Although ICH E15 and E16 and local guidance describe some principles for the regulatory evaluation of genomic biomarkers, there is currently no guideline on good genomic biomarker practices.

Guidance on good genomic practices will maximize the information gathered from genomic studies and facilitate the implementation of pharmacogenomics in drug development and patient treatment to the benefit of all stakeholders.

2. Problem statement

The progress of technologies generates new knowledge on potential association of genomic biomarkers of health and disease at an unprecedented speed in science: however translation of this information into clinical tools currently lags behind. In particular lack of transparent rationale for the choice of genomic techniques, difficulties in obtaining sufficient samples to address clinical correlations[i] and from the genomics perspective poorly designed clinical trials in many cases lead to non-reproducible and clinically non-validated biomarker data, highlighting the potential of genomics but slowing down the delivery of clinically usable tools.

3. Discussion (on the problem statement)

Open and shared guidelines harnessing transparency, consistency, reproducibility and even cross-validation of pharmacogenomics studies will facilitate delivering genomic biomarkers contribution to truly personalised medicines and facilitate early detection.

Guidance is needed to promote the choice of appropriate genomic methodologies during the development and the life-cycle of a drug so that the data accrued can be integrated to generate useful pharmacogenomics testing modalities. Once the principles for a robust clinical genomic dataset are discussed, the guideline would also highlight key scientific aspects for the translation of the available genomic biomarker data into clinical practice. Good Genomic Practices may also be a useful reference at the time when the new legislation governing companion diagnostics, in house testing and medical devices come into force in Europe.

It is proposed to produce a guideline to further discuss the following aspects:

1. Technology
    a. Choice of technologies used

b. Rationale for using the selected technologies

c. Standards (comparability) of technologies used

d. Analysis and reporting

2. Biomarkers implications on Clinical Trials

a. Justification for using genetic investigation

b. Identification of the clinical phenotype

c. Considerations for dose selection and drug regimen

d. Consideration of multiple markers, functionality, and significance

4. Recommendation

The Pharmacogenomics Working Party (PGWP) of the Committee for Human Medicinal Products (CHMP) recommends drafting a Guideline on good genomics biomarker practices.

5. Proposed timetable

- August 2014: CHMP adoption for 3 months' public consultation (deadline for comments by mid of November).

It is anticipated that a draft guideline will be available 9-12 months after the end of the public consultation of the concept paper and will be released for 6 months of external consultation, before finalisation.

6. Resource requirements for preparation

Development of the guideline will be led by the PGWP supported by EMA scientific secretariat.

A multidisciplinary drafting group will be appointed with representation from the relevant parties including Committees or Working Parties, e.g. Scientific Advice Working Party (SAWP).

Drafting work will be conducted primarily by email and teleconferences. 2 Rapporteurs will take the lead. The PGWP will discuss draft versions at its regular (plenary) meetings.

7. Impact assessment (anticipated)

The recommendations about the key pre-analytical, analytical and post-analytical issues associated with genomic biomarkers together with the rationale and design for genomic-driven clinical studies, will increase transparency, understanding and studies reproducibility for more efficient clinical validation of genomic biomarkers and ascertainment of their utility in clinical care.

Recommendations covering principles for incorporating genomic data and biological samples sourcing in clinical studies may be a useful tool in the dialogue with ethics committees and with subjects to be included in the study and could help to ensure that the genomic sampling is of adequate quality and a representative sample of the study population selected: on this basis data generated may be useful for the subjects involved and to contribute to advances in public health.

8. Interested parties

External consultation: pharmaceutical industry, academic centres of excellence in genomics; clinical labs (i.e. CLIA), diagnostics industry and genomics service providers; patients' organisations and social scientists.

9. References to literature, guidelines, etc.

- Draft Guideline on key aspects for the use of pharmacogenomics methodologies in the pharmacovigilance evaluation of medicinal products (http://www.ema.europa.eu/ema/doc_index.jsp?curl=pages/includes/document/document_detail.jsp?webContentId=WC500160232&murl=menus/document_library/document_library.jsp&mid=0b01ac058009a3dc)
- Guideline on the use of pharmacogenetics methodologies in the pharmacokinetic evaluation of medicinal products (http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2012/02/WC500121954.pdf)
- Reflection paper on methodological issues with pharmacogenomic biomarkers in relation to clinical development and patient selection (http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2011/07/WC500108672.pdf)
- Reflection paper on co-development of pharmacogenomic biomarkers and assays in the context of drug development (http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2010/07/WC500094445.pdf)
- Reflection paper on pharmacogenomic samples, testing and data handling (http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003864.pdf)

[i] Clin Pharmacol Ther 89: 529, 2011