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

Introduction

Pharmacogenomics (PG) is a rapidly evolving discipline that has the potential to significantly improve the discovery, development and use of medicines. To date each of the ICH regions have published some PG specific guidances or concepts and are in the process of developing others. However, there is no common set of PG terminology and this raises the potential for inconsistent use of terms in regulatory documentation and guidances and/or inconsistent interpretation by regulatory authorities, ethics committees, research participants and sponsor companies. The agreement on a consistent PG terminology at this stage will greatly facilitate the integration of this evolving science into global drug development and approval processes. There are no other international organizations that we are aware of currently working to resolve this issue. However, we would advocate informing key groups that the ICH is currently undertaking harmonisation of PG terminology to encourage future reference to any ICH PG output.

Agreed template for ICH Business Plan.

1. The issue and its costs

- *What problem/issue is the proposal expected to tackle?*

  The agreement on a consistent terminology for certain key PG terms will greatly facilitate the integration of pharmacogenomics into drug development, approval and clinical practice. It will provide the foundation for the development of future regulatory documentation at individual regulatory authority, regional and ICH levels. It will encourage consistent use and interpretation by the sponsor companies, regulatory authorities, ethics committees and research participants. The following terms will be addressed in this business plan:

  1. **PHARMACOGENETICS AND PHARMACOGENOMICS**
  2. **SAMPLE AND DATA CODING**
  3. **GENOMIC BIOMARKERS**
     Note: Although terms for sub-types of genomic biomarkers will be addressed, validation criteria for these sub-types will not.

- *What are the costs (social/health and financial) to our stakeholders associated with the current situation or associated with "non action"?*

  The lack of a consistently applied and interpreted terminology results in:

  1. Increased workload (and hence) costs to sponsor companies due to the requirement for multiple country, and even centre specific documentation, increased number of queries from regulatory authorities and ethics committees (resulting in study delays which average a couple of weeks to 2 months). This may impact small and medium sized companies even more than larger companies - for example in situations where fewer multi-country studies are run and hence country specific resource may not be available.

2. Increased workload for regulatory authorities and ethics committees as additional reviews of documentation is required to ensure clear understanding of protocols and informed consent documentation. This will require additional review time at ethics and regulatory review committees.
3. Reduction in the quality of research which can be conducted, as difficulties in collecting samples results in reduced sample sizes and hence power to detect pharmacogenomic effects. This may lead to either a lack of incorporation of pharmacogenomics into drug development programs, delays in pharmacogenomic research until post approval, or the conduct of sub-optimal research, again delaying or even missing the clear identification of a PG - associated therapeutic benefit in a given patient population.

Whilst it is difficult to quantify this in terms of financial or human costs, sponsor companies have employed dedicated staff and developed specific processes just for the logistical integration of pharmacogenomic sampling in clinical trials. A common terminology would reduce this burden of this work, significantly freeing up resource to work on the scientific application of pharmacogenomics. A continuation of the current situation will lead to a delay in, or even prevention of, patients receiving the benefits this science could bring.

2. Planning

- *What are the main deliverables?*
  A guidance document delineating an agreed basic terminology, which will be consistently interpreted in the 3 ICH regions. The terms which have been agreed upon for harmonisation are:
    1. **Basic definitions of pharmacogenomics and pharmacogenetics.** These terms are used broadly in the scientific and regulatory literature but with little consistency. Whilst establishing a single consistent definition across all scientific and regulatory stakeholders is unlikely in the short to medium term, the agreement of a consistent definition between ICH regulatory and industry partners would be a significant step forward.
    2. **Terminology describing the methods of coding for collection and storage of both DNA samples and genetic data.** Agreement of these terms and associated definitions will be especially helpful to groups reviewing clinical protocol documentation and informed consent. Broad principles of the regulatory implications of each defined term for sample/data coding and storage will also be included.
    3. **Terminology describing genomic biomarker attributes.** This definition will focus on attributes that are specific to genomic biomarkers and will not expand these definitions to non-genomic biomarkers. Input will however be obtained from other ICH groups working in this area to ensure that any proposed definitions are in line with other proposals and work streams. **Note:** The criteria for establishing validity of genomic biomarkers will not be included in this guideline, although an assumption that such criteria could be developed will be necessary. The regulatory implications of the categories of genomic biomarkers will also remain out of scope. These areas are important for the future implementation of pharmacogenomics and as such may represent topics to be addressed by this group in the future. This initial terminology guideline is an essential first step in the process of addressing these other important areas of work and ensuring a consistent implementation of pharmacogenomics and its presumed benefits globally.

- *What resources (financial and human) would be required?*
  Total of fifteen persons: Two persons from each of the six ICH parties and one observer each from Canada, WHO and EFTA.
  Four meetings of the Expert Working Group
  $30,000: $500 times 15 persons times 4 meetings

- *What is the time-frame of the project?*
  Two years

- *What will be the key mile-stones?*
  ICH STEP 2: 4th quarter of 2006
  ICH STEP 4: 4th quarter of 2007

3. The impacts of the project

- *What are the likely benefits (social, health and financial) to our key stakeholders of the fulfilment of the objective?*
  The anticipated benefits of this work are the consistent use of terminology by sponsor companies and regulatory authorities when developing PG -related clinical study and regulatory documentation, which should reduce the need for additional country and site specific documentation, and queries generated from these documents due to uncertainty around terms used and their implications.

  This will also provide a foundation which can be used if/ when future guidances are developed and reduce the number of queries generated to ensure clarity.

  The project will ultimately facilitate and accelerate the application of pharmacogenomics to benefit the patient as it will improve sample collection globally.

- *What are the regulatory implications of the proposed work – is the topic feasible (implementable) from a regulatory standpoint?*
  This work will benefit regulatory agencies. Having common definitions will serve as a basis for successful dialogue between interested parties. A common language will lead to increased efficiency and consistency of review of applications. For example, such consistency will ultimately give clarity on how samples labelled and coded in a specific manner, may or may not be used for drug label claims. Agreement on this subject for pharmacogenomics will lead to consistency in regulation in different regions. A protocol for sample labelling and coding is feasible from a regulatory standpoint.

4. Post-hoc evaluation

- *How and when will the results of the work be evaluated?*

A questionnaire based assessment could be performed evaluating the clarity, use and interpretation of the terminology by relevant bodies such as regulatory authorities and sponsor companies. A review of sponsor trial documentation and regulatory guidances could also be performed to assess compliance/ability to comply with the terminology. This assessment should be performed in 2008.