ICH

INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

Final Business Plan
E16: Genomic Biomarkers Related to Drug Response:
Context, Structure and Format of Qualification Submissions[*]
17 April 2008
Endorsed by the ICH Steering Committee on 11 April 2008[**]

Introduction

PG biomarkers are being increasingly used to aid drug development and regulation e.g. early decision making, dose selection, support drug approval and identify sub-populations with differing benefit-risk ratios. Dose selection and identification of patient sub-groups are important aspects for regulatory decisions and commonly agreed upon standards and formats for PG biomarkers are needed to facilitate the use of PG biomarkers in drug development and regulation. Although PG biomarkers are used for a range of applications each of which may require different levels of evidence to establish qualification for use, the standards and formats for submitting information about PG biomarker data to regulators should remain the same. Agreement on general principles for the types of data submissions required would allow consistent data packages to be produced by sponsors and facilitate data sharing by regulatory authorities. A standardised data format and content would add further to a consistent approach to biomarker qualification among the Regions.

Agreed template for ICH Business Plan

1. The issue and its costs

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

The future ability to qualify biomarkers for specific uses is of extreme importance to the industry as part of their efforts to increase the efficiency and reduce the costs of drug development.
Currently, regulatory processes for the qualification of a PG biomarker for a specific use are being initiated in the Regions. A key step in gaining qualification of a PG biomarker is to assure proper formatting of the data needed for qualification based on agreed standards. Emphasis is given to the global implications of such processes.

However, consistent data standards do not exist at the present time, despite the dramatic rise in exploratory PG research in drug development and the increasing submissions of such data to regulatory agencies. Different formats of PG data being submitted to regulatory agencies in different ICH regions can make it difficult for regulatory agencies to have discussions among them about qualifying biomarkers for an intended use.

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[*] In June 2008, the E16 name was changed from "Pharmaco Genomic (PG) Biomarker Qualification : Format and data standards" to "Genomic Biomarkers Related to Drug Response: Context, Structure and Format of Qualification Submissions".

[**] Endorsed by the Steering Committee on 11 April 2008, subject to amendments which have been included in this version dated 17 April 2008.

Therefore, there is a critical need within ICH to discuss and agree on the data standards and formats that should be used both for submitting PG biomarker data to regulators, and for exchanging information on the PG biomarkers during a qualification process.

Such an ICH guideline on PG Biomarker qualification data standards and format will facilitate harmonization, exchange of information and reduce the uncertainty that currently exists in the important area of PG biomarkers use and regulation.

The principles may also pave the way for further harmonisation on other technologies areas, where biomarkers may play a major role in facilitating development of innovative medicines

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

    The lack of consistently applied data standards and format results in:

    1. Delays in the application of PG biomarkers to drug development programs and reduced use of PG biomarkers in drug development pipelines;

    2. Increased resources required to prepare documentation and data for submission packages intended for regulatory review for biomarker qualification. This will increase the costs and delay the utilisation of biomarkers in drug development;

    3. Increased resources and longer review times required for assessment of biomarker qualification which will delay the application of biomarkers to drug development and potentially into clinical practice.

2. **Planning**

What are the main deliverables?

An ICH guideline delineating agreed data standards and format of documentation needed for the regulatory submissions aimed at the qualification of PG biomarkers for a specific purpose. The proposed guideline will result in an harmonisation process carried out through the discussion of case studies aimed to reach agreement on key principles defining:

❖ **Agreed formats.** Whilst it is clear that the evidence base required to demonstrate that a PG biomarker is qualified for a particular purpose will differ depending on context and intended use, and shall be evaluated on a case by case basis (and is not the topic of this proposal), the structure of the data submission and of accompanying documents will facilitate the processes by which that data is reviewed in the Regions. In addition, the use of agreed standards would allow regulatory agencies to combine data sets from differing submissions to improve their confidence and consistency in decisions about biomarker qualification. This will also support consistency across qualification processes within and among the Regions.

    Globally agreed data formats and standards would help ensuring the delivery of consistent, high quality submissions from sponsor to regulatory agencies, will facilitate international cooperation and reduce review time and resources required.

❖ **Agreed data standards**.   Agreed data standards would allows the development of standardised data storage, access solutions and analysis tools. This would reduce the time required for programmers / data managers to work with the data prior to it being available for regulatory reviewers and hence speeding up review times.

❖ **Agreement on how to define the qualification context and the claims for intended use.** PG biomarker qualification requires an accurate definition for the context and claims for intended use in line with data available to support this qualification. An inherently incremental process of biomarker qualification reflects the incremental generation of qualification data to support expanded context and claims.

It is important to also stipulate what is not in the scope of this new proposal. Issues that **will not** be addressed in the proposed guideline include:

- The regulatory process to be applied to accept PG biomarkers (e.g., for use as diagnostic tests);

- Use of qualified PG biomarkers in Marketing Authorization regulatory decisions (e.g., use as surrogates for clinical efficacy);

- Qualification and content/format for submission of non-PG biomarkers.

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, EFTA and WHO. Representation from interested parties (BIO, IGPA, WSMI) will be considered as appropriate. Five meetings of the Expert Working Group will be necessary to reach step 4 of the ICH process.

What is the time-frame of the project?

Three years

What will be the key mile-stones?

STEP2: Autumn 2009
STEP4: Autumn 2010

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 more rapid and efficient qualification of biomarkers driving their use into drug development. Consistent and clear data standards and formats agreed by all parties will reduce across the Regions the resources required to generate the necessary data for biomarker qualification. The standardised submission package and tools can be developed so that a single submission can be used in all regions. For regulatory authorities the benefits will include reduced resource required per submission and an ability to easily combine data and review either across submissions within the authority or across authorities.

  The increasing use of PG biomarkers in drug development will lead to several benefits e.g. improved early decision making and dose selection allowing early termination of

projects offering no benefits, while improving efficiency of later stage development by ensuring appropriate doses are used in phase 2b/3. This will increase the productivity of the pharmaceutical industry and lead to the availability of more novel therapies targeting unmet medical needs.

Consistency of data standards and formatting will facilitate the convergence of qualification processes and a more rapid acceptance of qualified biomarkers across regulatory regions reducing review times and resources required by each region. This will help speed innovative new medicines to patients in all areas.

- *What are the regulatory implications of the proposed work – is the topic feasible (implementable) from a regulatory standpoint?*

  No major impact on the regulations of each region

4. <u>Post-hoc evaluation</u>

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

There is an expectation that an increase in the number of these applications will be seen over the next 5-10 years. If harmonization is successful the quality of the documentation submitted by sponsor companies will increase with the time, and resources required to review them should decrease. An assessment of the suitability of the developed standards for PG biomarkers qualification purposes will be possible as regulatory authorities review applications for PG biomarker qualification.

An assessment will be made documenting the impact of the guideline in supporting the implementation of qualification processes at a global level, the resource required to review the applications and the time taken to provide that review: a survey of the experience gathered will be reported to the ICH SC within three years from the formal implementation of the planned ICH Guideline.