

APV Focus Group Drug Regulatory Affairs

International Association For Pharmaceutical Technology

Newsletter, **Issue 1/2010**

Editorial

The APV Focus Group Drug Regulatory Affairs considers itself to be a forum for an open scientific discussion of any issues relevant from a regulatory point of view within the field of marketing authorisation and pharmacovigilance of medicinal products. In this context we would like to inform you about current developments and draw your attention to APV events in a newsletter which will be issued on an irregular basis for the time being. Interested readers are welcome to provide proposals as to which topics the Focus Group should address and/or comment on. Please send your suggestions to the e-mail address of the Focus Group. Of course any kind of feedback and proposals concerning the contents of the newsletter and events organised by the Focus Group will also be appreciated.

Your Focus Group Members

International Conference on Harmonization

ICH Q8, Q9 and Q10 – background and work of the ICH Implementation Working Group (IWG)

Jean-Louis Robert

In 1990, 20 years ago, the International Conference on Harmonization (ICH) has started its activities. The objective was to achieve technical and scientific harmonization in registration for marketing authorization between Europe, Japan and the United States.

The experts are coming from the Regulatory Authorities of the European Union (EU), of the Ministry of Health, Labor and Welfare (MHLW) and of the Food and Drug Administration (FDA) and from Industry associations: European Federation of Pharmaceutical Industries and Associations (EFPIA), Japan Pharmaceutical Manufacturers Association (JPMA) and Pharmaceutical Research and Manufacturers of America (PhRMA). In addition, observers are coming from Health Canada, Swissmedic, World Health Organization (WHO) and International Federation of Pharmaceutical Manufacturers and Associations (IFPMA). If initially the scope of ICH was new chemical entities and biotechnology derived products, it became clear with the time that the requirements described in the initial published guidelines were equally important for known/existing active substances. Therefore International Generic Pharmaceutical Alliance (IGPA) and World Self Medication Industry (WSMI) joined the process as interested parties (see also www.ICH.org).

In addition in Europe, the regulators (e.g. stability, impurities) and the European Pharmacopoeia (the general monograph "Substances for pharmaceutical use") have already applied these concepts and principles described in the ICH guidelines for existing/known active substances and corresponding products.

At the beginning of ICH guidelines addressed the following topics: stability, analytical validation, impurities, specifications, common technical document, GMP for active pharmaceutical ingredients.

In 2002/2003, the ICH Steering Committee asked the Quality experts to define the future vision in pharmaceutical quality. After some discussions, this has ended in the following statement in Brussels, in July 2003:

"Develop a harmonized pharmaceutical quality system applicable across the lifecycle of the product emphasizing an integrated approach to quality risk management and science".

The guidelines which describe this new paradigm in quality are:

- Q8 (R2): Pharmaceutical Development
- Q9: Quality Risk Management
- Q10: Pharmaceutical Quality System
- Q11: Development and Manufacture of Drug Substances (chemical/biological entities): in progress

Q8R2, emphasizes on the importance of pharmaceutical development in order to ensure that a medicinal product of consistent quality is released on the market. It also provides guidance, which additional opportunities in manufacturing flexibility are possible (e.g. real time release testing, design space) when performing an enhanced development program providing more product and process understanding, especially interaction between and among critical process parameters and critical quality attributes.

Q9 provides general guidance on different risk management tools which can be used in the pharmaceutical area including pharmaceutical development. It does not promote one tool against another; it also indicates that a manufacturer can use its own risk management tool. The more formal use of risk management will help Industry to better identify for instance CPPs and CQAs, to better retrospectively reevaluate their development process and the Regulators to better understand the applicant's approach and/or strategy to development and manufacturing of its product.

Q10 is in principle not new requirements. A Quality System, under GMP, has in all cases to be implemented. However a Q10 type quality System promotes in addition two key enablers, Pharmaceutical Risk management and Knowledge Management, and addresses the lifecycle approach.

This new paradigm can be summarized as follows:

Science is no longer isolated; it is living across the lifecycle of the product/process within an efficient Quality Management System. This allows a better utilization of modern technology. Appropriate implementation of knowledge management will facilitate continual improvement of product and process throughout product lifecycle.

Following the adoption of these three guidelines and to ensure a harmonized implementation, the ICH SC installed an implementation working group with the following main tasks:

- Communication and training
- Technical issues and documentation
- Influence of this new paradigm on existing ICH guidelines

A series of Q&As on different topics (design space, real time release testing, quality system) have been published so far and can be seen under the ICH website.

Stakeholders are encouraged to submit any question they may have on the implemen-

tation of the three ICH guidelines not yet covered by the published Q&As to the IWG via the ICH website (www.ich.org).

Three training workshops (Tallinn (Estonia) June 2-4, 2010; Washington October 6-8, 2010; Tokyo October 25-27, 2010) have or will take place in order to further pass the message around the implementation of Q8, 9 and 10. They are based around one case study and address development (industry speaker), assessment (regulator: assessor speaker), manufacturing (industry speaker) and inspection (regulator: inspector speaker).

Breakout sessions (BOSs) around different topics design space, control strategy, quality risk management and pharmaceutical quality system will take place and allow discussion between Regulators and Industry. The outcome of the BOSs will be used in order to further facilitate the implementation of these concepts and principles described in these three guidelines.

Conclusion

One of the objectives of the three guidelines (Q8, Q9, Q10) was to facilitate the introduction of new technology in the pharmaceutical field and to show which opportunities (regulatory flexibility) can be reached when applying the principles and concepts therein described. These principles will also be the basis for applying for the "Post approval change management protocol" as foreseen in the EU Variation Regulation EC 1234/2008.

The ICH IWG is organizing training workshops, bringing together industry and regulators from all over the world, and publishes Q&As to facilitate the implementation of the new quality paradigm.

Disclaimer: This newsletter is provided "as is" and without warranty, express or implied. All warranties with regard to the accuracy, reliability, timeliness, usefulness or completeness of the information contained in the newsletter are expressly disclaimed. All implied warranties of merchantability and fitness for a particular use are hereby excluded. None of the information provided in the newsletter constitutes, directly or indirectly, the practice of medicine, the dispensing of medical services, the recommendation to buy or use a product. External links are provided in the newsletter solely as a convenience and not as an endorsement of the content on such third-party websites. The APV Focus Group Drug Regulatory Affairs is not responsible for the content of linked third-party sites and does not make any representations, warranties or covenants regarding the content or accuracy of materials on such third-party websites. If you decide to access linked third-party websites, you do so at your own risk.