PRINCIPLES OF ANALYTICAL QUALITY BY DESIGN FOR THE DEVELOPMENT OF QUALITY CONTROL METHODS IN A PHARMACEUTICAL CONTEXT

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Pharmaceutical regulatory agencies increasingly require the implementation of systematic approaches covering the entire life-cycle of pharmaceutical products, from manufacturing processes to quality control tests. In 2009, the International Council for Harmonisation (ICH) of technical requirements for pharmaceuticals for human use proposed a systematic approach named "Quality by Design" (QbD) to be implemented in the pharmaceutical field [1]. In this context, the QbD strategy have been progressively applied also to other aspects of the pharmaceutical chain, such as the analytical method development in quality control laboratories. The QbD applied to analytical chemistry is commonly named "Analytical Quality by Design" (AQbD) and in the last decade it has been widely applied in academia for the development of separation methods, involving different techniques such as LC, CE as well as SFC. However, its implementation in quality control laboratories still remains limited and then its advantages not completely exploited. Indeed, this approach presents a lot of conveniences, such as the deep knowledge acquired during the method development/optimisation by studying how critical method parameters (CMPs) affect critical method attributes (CMAs). Moreover, this strategy allows the possibility to define a method operable design region (MODR) consisting of a multitude of possible working points and for each of them a specific probability of success (π) is given. Indeed, the concept of risk plays a central role in this strategy as the MODR is considered of a zone of theoretical robustness limited by the so-called edges of failure, outside which the method performances are not accepted [2]. This presentation focuses first on the theoretical aspects regarding each step of this strategy. The analytical target profile definition, the selection of CMPs and CMAs, as well as screening and optimisation of CMPs and MODR definition are accurately described and illustrated. Some considerations about the choice of the working point, its validation and the planning of an efficient control strategy are also given. In the second part of this presentation all these

concepts are once again showcased but from a practical point of view, by giving two concrete case-studies following the AQbD approach. The first one concerns the development of a liquid chromatography coupled to UV (LC-UV) method aimed at quantifying the cannabinoids content in cannabis extracts used for medicinal purposes [3]. The second one shows the approach applied to the development of a stability indicating method by using another analytical technique, the supercritical-fluid-chromatography coupled to mass spectrometry (SFC-MS). This latter is intended to be used for the quantification of hydro-soluble vitamins and amino acids in a complex medium.

References

[1] ICH Harmonised Tripartite guideline. Pharmaceutical Development Q8(R2) (2009) International Council for harmonisation of technical Requirements for Pharmaceutical for Human Use.

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