Application of Analytical Quality by Design to Pharmacopoeial Methods

Stakeholders are invited to comment on the draft supplementary chapter for the application of analytical quality by design to pharmacopoeial methods.

This chapter is not designed to be mandatory and is to be provided as selective guidance for the application of Analytical Quality by Design principles to pharmacopoeial procedures and across the entire Analytical Method Lifecycle. It is intended that the British Pharmacopoeia, together with its expert working party, will add to and revise this guidance as internal and external knowledge grows and further international standards are developed.

Details for the public consultation of this monograph are as follows:

WP - AQbD	**Working Party - Analytical Quality by Design**
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Deadline for Comment	30th April 2021
Target Publication (subject to change)	BP 2022
Notes:	**NEW SUPPLEMENTARY CHAPTER**

In addition to seeking comments on the document itself, stakeholders are invited to consider the following specific questions in responses to the consultation.

1. Do you/your company have a working knowledge of Quality by Design concepts and their application to analytical methods

2. Do you/your company work with pharmacopoeial methods regularly? In what capacity

3. Does this Supplementary Chapter help to inform you or your analysts on the value of applying AQbD to pharmacopoeial methods? Why? Why not?

4. Please suggest additional content, revisions and improvements that would enhance the value of this supplementary chapter.

5. What additional information, guidance and training would be useful in enabling understanding and adoption of analytical quality by design by users of the pharmacopoeia?

understand the influence of variability on method parameters (e.g., temperature, solvent composition, etc. for an HPLC method) on the results generated by the method, as well as the effect of typical changes in method conditions that can occur over time and across laboratories (i.e., instrument type/design, reagent quality, sample shakers, analyst training, etc.)

Pharmacopoeial methods are intended to be applicable to a wide range of available formulations and this often requires review of data and laboratory evaluation of submitted, registered methods to ensure the methods are suitable for pharmacopoeial use. This process includes application of quality risk management principles and tools to focus the investigation of the most critical aspects of the method and maximise the knowledge gained from laboratory work.

The case study performed by the MHRA and the BP applied the following principles in a step-wise process in order to learn their how they can be applied effectively to pharmacopoeial procedures. The aim of this work was to demonstrate that AQbD can be used to ensure robust and fit-for-purpose methods being produced in the BP. The case study showed the value of their application to an Assay procedure and the BP is continuing to apply and further investigate the learnt principles to a range of pharmacopoeial procedures.

3. Quality Risk Management for Analytical Procedures

The process of building method understanding begins during method development and continues through the formal validation (in line with conventional ICH Q2: Method Validation), verification and method transfer exercises and routine use, including with pharmacopoeial methods. Historically, the BP has utilised risk management principles to inform the laboratory evaluation of analytical methods. The outcomes of the AQbD case study have been used to enhance this process.

Users of the pharmacopoeia may not have prior knowledge of a given method, above and beyond what is detailed in the pharmacopoeia. This section summarises the application of quality risk management tools, including risk assessments, to analytical methods in the pharmacopoeia.

Prior knowledge, such as information contained within monographs, supplementary materials in pharmacopoeias, or information in the literature can be leveraged if available. Quality risk management (QRM) tools (See ICH Q9[2]) provide a framework for identifying, studying and understanding the risks to method performance and the results generated by the method. The QRM tools are most effective when initiated during method development or evaluation and applied iteratively. This allows inclusion of the most recent knowledge and reassessment of risks based on any new understanding.

Method development should involve a systematic screening of method conditions, including sample preparation, to identify a set of conditions as a starting point for further evaluation via risk assessments and the QRM process. In the case of a compendial method where formal method development may have been performed by the collaborating manufacturer or by an external laboratory, initial screening of method conditions (for example, screening DoE's –

[2] https://database.ich.org/sites/default/files/Q9%20Guideline.pdf

Draft Monograph – Subject to change