Table 2: Analytical Method Life Cycle Management and the Revised ICH Q2 and New ICH Q14

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Scope:
Analytical method development can be performed in a traditional approach or using risk based development approaches in analogy to the concepts described in ICHQ8 to ICHQ11 for process and product development may be applied. ICHQ14 guidance document was initiated with the goal to align and to better describe elements of method development and how enhanced method development concepts may contribute to more robust methods. Opportunities to present method development data in filing documents should be explored but also in what extends this could facilitate efficient and science-based change management by improving communication between industry and regulators.

ICHQR2 provides guidance on the validation of analytical procedures to demonstrate its suitability for the intended purpose. It presents a discussion of the characteristics to be considered consideration during the validation of the analytical procedures and to be included as part of registration applications. Where the document can be easily applied to analytical procedures based on e.g. chromatography, the current Q2(R1) however does not adequately cover more recent application of analytical procedures, (e.g., Near Infrared (NIR) Spectroscopy, Raman Spectroscopy, immunoassays or cell based assays). The current approach of Q2 (R1) is not sufficient to establish the suitability of methods relying on multivariate data.

Questions for Discussion:
1. How is method development guided to ensure consistent output and robust methods?
2. What are potential elements contributing to an enhanced analytical development approach?
3. How are performance targets described before the start of method development?
4. What is an Analytical Target Profile and what could it describe?
5. What is a Method Operable Design Region (MODR) and how could it be established?
6. What are potential benefits using an ATP concept?
7. What risk management principles could be applied during method development?
8. How to derive a method control strategy
9. How to ensure continuous method performance?
10. Where do you see need for change with the existing ICHQ2(R1) guidance?
11. What are the essential elements of ICHQ2(R1) which should be maintained?
12. What technologies require method validation where guidance from ICHQ2(R1) is limited?

Discussion Notes:

- People from various companies and research centers joined the round table on ICHQ2 and ICHQ14. Mr. Christof Finkler (facilitator) is member of the expert team of ICH.
- ICH comprise people form agencies like FDA, EMEA and industry and include guidelines for small and big molecules.

- It was discussed that to address risk assessment, first of all critical parameters should be defined and most of the time it is based in prior knowledge or historical data.
- For method qualification, a predefinition of the expectations was considered an important point (e.g. aim of the assay, screening or stability purpose…). The question raises who is defining the expectations.
- Some parameters have predefined values (ranges) by pharmacopeia while in other ones the ranges are defined after collection of large set of data. When biological impact is encounter the ranges should be more strict.
- The connection between ICH 8,9,11 is based on PK studies and certain CQAs. This defines the importance of certain parameters and how strict the borders need to be set.
- Analytical target profile is hard to apply for certain aspects. It is mainly used for chromatographic separations (*e.g.* IEX: goal to detect as much impurities as possible), but also for potency assays.
- In early stage development there are not clear lines on what requirements need to be fulfilled and, therefore, establishment of an appropriate ATP may be difficult. Previous knowledge from similar topics was found to be the most useful.
- ICHQ14 try to provide a solution to the previous points and to serve as a guideline. ICHQ14 should not add more requirements. It was comment that it would make sense to include it in the dossier which is sent the agencies.
- Using methods from a monograph is easier to implement (only quick validation necessary) then bring in a completely new method.
- Enhanced method description leads sometimes to problems, for example to many details in dossier leads to no possibility of adapting certain parameters after. (*e.g* for CE methods every Kit and reagent is defined, or HPLC vendors). Instead, the focus should be on the critical factors and the border of these ones should be defined more strict.
- It was unanimously agreed that QbD has helped and enhanced method development.
- QbD may include your pre-validation data combined with method development in order to limit the risk that your method fail during validation. If this risk is already excluded in the method qualification, the pre-validation could also be skipped and directly the method validation could be done.
- First the CQAs are defined and which factors have an high influence on the method. These defines then the parameters and limits for a DoE.
- It was discussed that if a DoE shows already that certain parameters are in the green range, these ones could be excluded during validation. Instead it would be better to focus only on critical factors.
- The ideal situation would be to have a checklist for each specific method, indicating which parameters should be tested during the qualification and which ones can have an influence or can be risky. This would prevent that important parameters are missed and the validation fails.

- To go even a step further, it was discussed that if a detailed qualification with GMP compliant data was already done, the validation could be omitted. This would prevent to do double work and will reduce the risk that a method will fail during validation.
- It was agreed that it is also important to asses why a validation failed. This enables to understand, which factor is important to include in a DoE and helps to avoid further methods failures during validation.
- ICHQ2 should be improved in the quantitative aspect of method validation.