Table 36: Practical Considerations for Implementing ICH Q14 for Each Drug Modality – Old and New

Facilitators –

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Scope:

Analytical procedures are necessary to help develop products and monitor the manufacturing process, measure critical quality attributes and to help ensure the quality of final products. These analytical procedures can be modified or improved throughout the product lifecycle because of continual improvement activities. This round table is intended to encourage discussion on practical consideration for implementation of ICH Q14 with respect to chemical modalities, analytical methods and control strategies.

A new guidance, ICH Q14 Analytical Procedure Development, is in development and its current status is step 1. The guideline will provide an opportunity to present the outcome of Analytical Procedure Development in both traditional and enhanced approaches (i.e., QbD models) and to facilitate identifying and then selecting operating conditions for methods. The guidance may also assist sponsors with information about model updates and re-validation experiments that reduce the regulatory burden of post-approval changes (PAC) with the goal to enable more efficient, scientifically sound and risk-based change management procedures.

Questions for Discussion:

1. How will Q14 be related to Q2 (R1) revision, and what will be the benefit if Q14 and Q2(R2) are combined?
2. How to align different aspects of AQbD (Analytical quality by design) /MLCM (Method lifecycle management) that are already present with Q14?
3. How will this new guidance apply to analytical methods for new modalities lack of prior knowledge?
4. How will Q14 be related to Q13, in terms of development of procedures for Real Time Release Testing (RTRT), validation of multivariate procedures, and application of process analytical tools (PAT)?
5. How will Q14 facilitate implementation of method improvements and novel technologies?
6. How are the requirements different if it is an entirely new type of test (*i.e.* no prior product specification) *vs* replacing an existing test for the product attribute?

7. What type of regulatory flexibility is the industry expecting for different modalities?

Discussion Notes:

January 26 and 28, February 1 and 3, *combined* –

What will be the advantage of analytical quality by design (AQbD)?

- AQbD should be a tool to make method development easier, not for more paperwork. Implementing AQbD will help to document decisions and visualize where a gap might be, which will in turn facilitate method optimization.
- When working according to the concept of AQbD, people can take a step back and think about the science behind the methods. This could prevent running into problems later on.
- Design of Experiments (DoE) is a very powerful tool, the key is still the science behind. If using wrong parameters or ranges, the DoE will not work.
- The implementation of AQbD is different for each firm. It is dependent on the culture of the organization and how the people in that organization work and deal with their knowledge.
- Implanting AQbD could really help keeping the focus on developing a fit-for-purpose method.

How could Q14 support accelerated development timelines?

- Predefined performance characteristics described in an ATP can facilitate technology selection and guide method development.
- Use of enhanced elements described in Q14 can result in better method understanding and hence less failure during transfer into QC labs.
- The use of prior knowledge can reduce development efforts for analytical procedure. Especially the establishment of platform methods is a powerful concept to speed up the establishment of the analytical control system.
- Working with CMO's the sharing of platform methods a validation data may be difficult.
- Validation efforts for platform methods may be reduced. This should not only be possible during clinical phases but also for marketing authorization.
- It was discussed how development data could be used to demonstrate adherence to validation characteristics in order to the generation of the same data during validation

Can the concepts described in Q14 be applied for new modalities?

- The principles described I Q14 can be applied in any modality.

- The QRM based development approach provides advantage in the field of new modalities where higher uncertainties exist, and often new technologies are required.

How to define "platform method"?

- The term platform method is being interpreted in different ways. It is seen as a starting

point for method development, or as a method which is validated for several molecules.

- The terminology of these kind of platform methods has changed over time. It started out with calling it method development strategies, then it changed to method development starting conditions, later generic methods, and now platform methods.
- Platform methods are usually applied for attributes which are common for several molecules derived from similar manufacturing platforms. Before use of a platform methods with a new product its suitability needs to be assessed.

What will be the documentation requirement by Q14?

It seems that Q14 is not intended to introduce new regulatory requirement. Documentation requirement will be provided in the draft and regulatory flexibility might depend on the scientific knowledge and justification provided by sponsors.