Table 3: ICH Q2(R2) / ICH Q14

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Scope:

The draft guidelines on analytical development and validation are promoting science and risk-based approaches in line with the systematic approach suggested in ICH Q8 and using principles of ICH Q9 for developing and maintaining analytical procedures. In particular, draft ICH Q14 describes principles to support change management of analytical procedures based on risk management, comprehensive understanding of the analytical procedure and adherence to predefined criteria for performance characteristics. In alliance with the principles described in ICH Q12, companies might get rewarded for applying the enhanced approach for analytical method development by gaining more regulatory flexibility in the post approval phase.

Questions for Discussion:

1. How will the enhanced method development principles described in ICH Q14 translate into an improved method understanding leading to more regulatory flexibility? What are the experiences gained so far in the field with the use of a method operational design region (MODR) and its connection to an Analytical Target Profile (ATP)?
2. How is the Analytical Target Profile embedded in the context of an overarching risk based Control Strategy? What product and process understanding is required to define a reasonable "Analytical Target Profile"?
3. Filing and adherence to a predefined ATP seems to be a key enabler for an enhanced analytical method lifecycle. How can a company demonstrate adherence to ATP? How can we use the Pharmaceutical Quality System (PQS) and generic bridging strategies to get an early agreement with regulators for not yet foreseeable analytical method or technology changes? How could a "generic" Post-Approval Lifecycle Management Protocol (PACMP) or Product-Lifecycle-Management (PLCM) document look like that is used to describe the "adherence to ATP" including a method bridging strategy? Will the approach be accepted by all regions or do we expect regional divergence e.g. in countries that do not have adopted concepts described in ICH Q12?

Discussion Notes:

- Discussion around expectations / experiences with using ATP / aQbD principles according to ICH Q14

- hope that guidelines will drive / foster the implementation of aQbD (extrinsic motivation) or rather guideline will describe the basic principles of purpose / science driven method development (intrinsic motivation)
- no experiences so far with filing of ATP, very limited experience with using it in development
- use of ATP requires different kind of thinking: purpose of method needs to be understood / i.e. define performance requirements to measure a specific CQA via the ATP
- ATP can also be applied to generic / platform methods
- connection of specification limits vs analytical method capability / variability: ATP to define performance requirements of the method
- science is key - basic understanding of method is required, could be simple things as e.g. sample preparation / use of replicates / appropriate dilution series
- regulatory expectation: streamline regulatory filings in terms of the to be provided supportive information

- Use of ATP in commercial space, for MAA/BLA filing
  - CQA centric thinking instead of method based thinking; direct link of method to safety and efficacy
  - ATP as contract / handshake (industry vs regulator, sponsor vs customer (CDMO) or developer vs management to justify re-development / claim additional budget
  - do it right first time, i.e. a suitable method is chosen from the beginning – less need for redevelopment during late stage development
  - business case: less troubleshooting & regulatory flexibility (change and variation filing)
  - technology switch post-approval currently not really possible -> need for more regulatory flexibility to foster innovation
  - difficult to predict the future change, therefore a specific change protocol does not really work
  - QbD related data not always seen by regulators - more company internal approach -> Do we need to make it more visible to regulators to get their buy in?
- Method trending / Analytical control strategy
  - learn from trending data although method performs still within limits
  - understand your method for your own benefit e.g. to intervene early on