Performance and Context Based Established Conditions for Analytical Procedures

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Introduction and Problem Statement

The different risk understanding in view of the regulatory assessment of a change results in country specific reporting categories (Figure 1)

- Pharmacopoeias have different understanding in view of adjustments and modifications. Raw material, drug product, and general monographs are not fully harmonized (e.g. dissolution step concepts of Ph.Eur and Ch.Phr.)
- Different Timelines and Requirements for regulatory change control processes are daily challenges for the regulatory lifecycle management of analytical procedures (Figure 2)
- Regulatory Compliance Oversight is nearly impossible and higher resources are needed to control the logistic complexity instead of facilitating continuous improvement

ATP - Definition, Example, and Terminology

For regulatory processes (e.g. Change Controls) besides the predefined method performance the related Regulatory Context has to be known and adequately described

ATP provides more regulatory background for an assay specification based on CRS (Clinically Relevant Specifications[2]). Taking into account allowed batch variability (e.g. ± 2%) and degradation rate of API, the total error has to be better than 1%

Figure 6 should stimulate discussions for the most challenging topic to switch between technologies for an “Related Substances ATP”. The Quality and reliability of the context description forms the basis to what extent operational flexibility can be implemented for impurity testing methods.

The Ph.Eur the monograph (e.g., 2.2.40 NIRS®) in conjunction with EMA Guidance EMEA/CHMP/CVMP/WP/17750/2009 (Rev2 already provides context and performance based conditions to be established)

Regulatory Context of an ATP (Examples for Assay and Related Substances)

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Level Concept for Established Conditions and Conclusion

In order to be able to proceed as “Do and Tell”, for method changes that involve a different analytical technique (e.g. moving from chromatographic to spectroscopic) three main regulatory elements may be required

- Performance based[4] Established Conditions: ATP for a specific CQA as part of the Control Strategy (ICHQ8)
- Regulatory Context based Established Conditions to enable the ATP as regulatory element (Risk and knowledge based approach ICH Q9, 10)
- Change Management Protocols: PACMP

Conclusion

The proposed Performance Based Level Concept[4] will work with ICHQ8 - 12 and intends to provide a framework to harmonize and facilitate the post approval change management in a more predictable and efficient manner (Figure 8)