Quality by Design for Analytical Methods for Use with Orally Inhaled and Nasal Drug Products

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While there are many common analytical unit operations and processes associated with OINDP methods, these will be identified with sample collection (Figure 2). Understanding method requirements - Developing the analytical target profile

On identifying the need to develop an analytical method to measure an OINDP attribute or process parameter the following points should be considered:

- The type of sample to be tested, e.g. in-process sample, formulation intermediate, raw material, packaging component, completed OINDP device and their known critical quality attributes.
- The proposed operating environment such as in-line or off-line on the manufacturing line of off-line within Quality Control and/or Development laboratories.
- The desired method cycle time.
- Any target criteria or specifications available from Pharmacopoeial or regulatory guidance.

Selecting and developing an optimum analytical method

Once finalised, the target profile can be compared with knowledge of the capability of different techniques to inform the selection of the apparatus and optimum operating parameters for each element of the method (i.e. sample collection, preparation and quantification, see below). Alternative ways of achieving the analytical target profile may be possible.

Additional aids in the identification of critical method parameters are standard risk assessment tools and management tools, such as cause and effect analysis (see Figure 4) and Failure Mode and Effect Analysis (FMEA).

Developing the method control strategy

Suitable controls for the critical analytical method parameters should be established such as instrument performance checks, run qualification procedures and method system suitability criteria to ensure the method requirements are consistently met.

Monitoring method performance and continual improvement

Suitable monitoring of critical analytical method parameters, for example a control chart, will result in ongoing trend assessment. Any interventions or improvements should use the established quality system to manage the associated change requests. Where technological advances result in new ways of achieving the established analytical target profile, again the quality management system should be used to manage the transition over to the new technology.

CONCLUSIONS

Measurement systems form an integral part of a quality by design development programme and the application of science and risk based approaches to analytical methods will result in better understanding, more robust, methods with better control of critical analytical method parameters. Sharing this increased knowledge with regulatory authorities should result in a decreased need for pre-approval of non-critical method changes and increased incentive for continual improvement.

Further discussions on the best way to share the increased knowledge associated with analytical methods in regulatory filings, exemplified via case studies, will be part of future efforts of the IPAC-RS Analytical Methods Working Group.

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