Analytical methods Quality by Design (AM-QbD) Risk Assessments undertaken within GlaxoSmithKline (World Wide Inhaled Product Development) for Orally Inhaled and Nasal Products

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Introduction

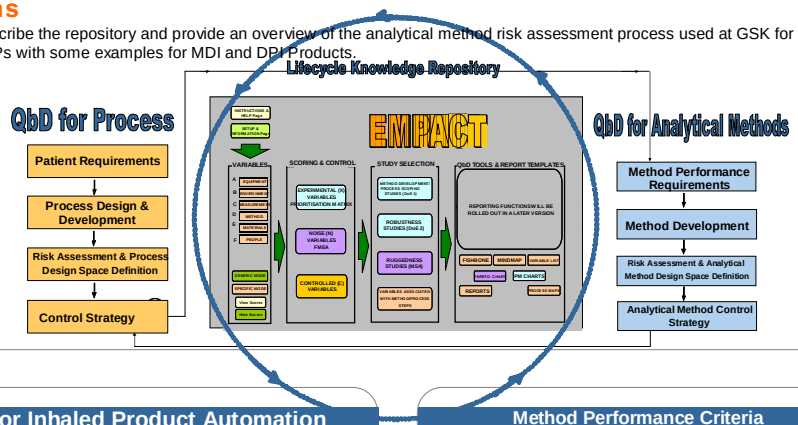
Fundamental to any method development is being clear on the design intent of the method. **Method Performance Criteria** and **Method Operational Intent** are two important aspects of this design intent.

Project Background

Throughout the lifecycle of a given Orally Inhaled and Nasal Drug Product (OINDP) method it is inevitable that there will be changes in the 'method environment' that can impact its operation. Changes/improvements to a method should be made with reference to a method knowledge repository. GSK's repository is entitled **EMPACT** (**Experimental Method Parameter Assessment Control Tool**).

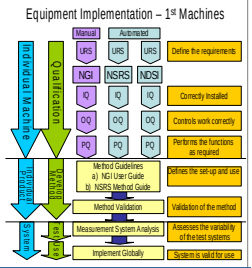
Aims

Ø Describe the repository and provide an overview of the analytical method risk assessment process used at GSK for OINDPs with some examples for MDI and DPI Products.



QbD for Inhaled Product Automation

- Cross inhaled Project application (automation MDI and DPI)
- QbD example for introduction of inhaled product automation has been presented to FDA
- Reduction of potential Analyst error using Automation

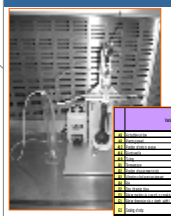


Semi-Automated NGI DPI Sample Solution Preparation

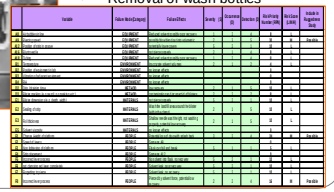
Method Performance Criteria

Method Performance Criteria are driven by an understanding of the process monitoring and control requirements and the ability to maintain the Product Design Space, i.e. the ability to meet the required critical quality attributes (CQAs). CQAs are identified, through a thorough understanding of those attributes of a drug substance or a drug product which may need to be controlled in order to assure the safety or efficacy of a product. This control can be achieved via specification limits, In Process Controls, in line monitoring and Process Analytical Technology etc. Method Performance Criteria are defined by using a rigorous approach for identifying all the potential method factors that need to be controlled to assure method performance and through the use of risk assessment tools and prioritised experimentation that eliminate areas of risk.

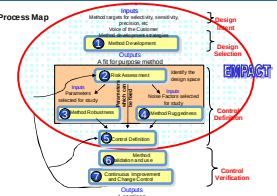
Blister Strip Apparatus (BSA)

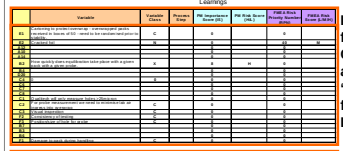


- Manual manipulation of the strip
- Controlled alignment of piercing
- Standardised process
- Sample recovery by pumped solvent
- Volumetric process
- Removal of wash bottles

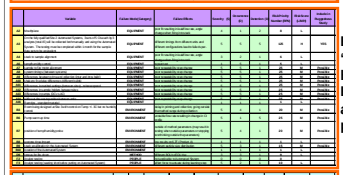


Process Map linked to DFM

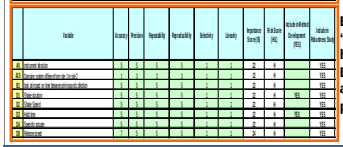




Inclusion of factors to be Controlled alongside ''X'' and ''N'' factors for a DPI product

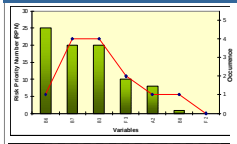


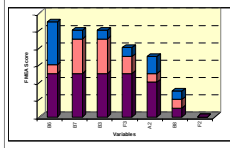
Example of ''N'' factors held in EMPACT for an MDI product



Example of ''X'' factors held in EMPACT for an MDI product

Outputs from Prioritisation matrices and FMEA exercises that come out of AM-QbD Risk Assessments held in EMPACT templates.





Any proposed changes that take the method outside its proven design space are risk assessed and for high risk changes an evaluation or equivalence exercise is performed to assure method performance criteria are still met. Method specific learnings are used to update the method knowledge repository. Technique learnings are used to enhance the risk assessment process for future methods. This is particularly important for automated methods for OINDPs.

Conclusion

As demonstrated, the AM-QbD Risk Assessment process for OINDPs has been fully considered to fully mitigate the analytical risk associated with testing OINDPs in different laboratories within GSK. Key to this process is the scoring system (for prioritising potential method factors that need to be mitigated) that has been developed, piloted and established within GSK R&D.

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