Summary - Matrices and Bracketing in Process Validation

Bracketing and matrixing allow a 'most appropriate challenge' condition to be defined for a process or drug product family (the same drug product with different dosage strengths). This risk-based approach can allow the validation to be focused on the most challenging circumstances, or "worst cases." Use of this approach can provide a significant benefit to reduce the overall validation effort. Bracketing or matrixing may be used for validation of Drug Product, Active Pharmaceutical Ingredient and Packaging processes when this approach can be justified.

Matrixing is typically used when there are significant similarities between products in a drug product family (e.g., same product different strengths in the manufacturing stage or different products with similar container closure in the packaging stage).

Examples of variables that might be assessed by bracketing and matrixing include, but are not limited, to:

- Batch size;
- DP dosage strength;
- Identical equipment (e.g. where setup and operating conditions are the same);

To obtain the maximum benefit with minimum risk from bracketing and matrices, it is necessary to have a well-developed understanding of the impact of critical process parameters on critical quality attributes. There should be a documented and justified rationale that explains why one set of test conditions (e.g., manufacturing process, product presentation, etc.) is representative of one or more related test conditions.

A new product will be transferred from one manufacturing site to another. The product is a capsule dosage form. A common blend is used to prepare five different dosage strengths. The packaging presentations and capsule sizes are shown in Table 2:

This example is one of matrixing of the different strengths and capsule sizes. We have solid dosage units with similar capsule size packaged with the same tools in the same type of container/closure (for those that use the same components). It is also an example of bracketing of packaging components for those dosages that have similar components (bottle/closure).

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