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Short communication

The difference between verification and validation of analytical methods in the pharmaceutical industry

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Introduction

To submit a dossier for marketing authorization to the Regulatory affairs, a product owner must provide Common Technical Documentation (CTD) containing a pharmaceutical product characteristics, manufacturing, quality control, safety (nonclinical), and efficacy (clinical) testing results before gaining approval for market access. Although quality improvement measures in the quality control laboratory have been enormous in recent years, especially due to improved handling of the validation and verification of the method performance, they often still differ widely from laboratory to laboratory. Much of what has been published on this topic is difficult to apply in routine laboratories due to complex statistics (Pum, 2019). The result is that method validation is often implemented incorrectly, which leads to false conclusions about the performance of the method, potentially compromising patient safety (Pum, 2019). The purpose of qualification, validation and verification is to generate reliable data for the products tested, resulting in the delivery of quality drug products to the patients (Ng, 2022). Therefore, the aim of this research is to emphasize the differences between verification and validation of analytical methods in the pharmaceutical industry.

Materials and methods

To achieve our goal, we used the following references:

1. ICH Q2R1: Validation of Analytical Procedures: Text and Methodology. Proceeding of the International Conference on Harmonization of Technical Requirements for the Registration of Drugs for Human Use, Geneva, Switzerland, 2005
2. ICH Q2(R2)/Q14 EWG - Analytical Procedure Development and Revision of Q2 (R1) Analytical Validation, 2022
3. ICH Q4A - Pharmacopoeial Harmonisation (Elder, 2017).

Results and discussion

Although method verification and method validation look similar, they are really not the same and have different requirements. An analytical method should be tested from different aspects to prove that the test results obtained by testing with this analytical method are reliable and we can trust them.

Analytical method validation

Various aspects of performance characteristics are required to be assessed during the method validation as (ICH Q2R1, 2005):

- **Accuracy:** an evaluation of how the result is related to the true value
- **Precision:** an assessment of repeatability on the multiple measurements, which shows the distribution of the results
- **Specificity:** to prove that the method can identify the desired component from the matrix components
- **Detection limit:** certain level (usually presented as concentration) set to determine how a method can

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distinguish the measured signal of sample from the noise

- **Quantification limit:** the lowest amount of sample (usually expressed as concentration) that can be quantified by the method with acceptable precision and accuracy
- **Linearity:** reflects how the test result is related to the concentration of analyte
- **Range:** an interval of different analyte concentrations between lower and upper levels that can be used for examination
- **Robustness:** an index of how a method is capable of remaining stable under small variation from the procedure

Analytical method verification:

Method verification is an assessment that focuses on the suitability of an analytical test procedure for its intended use in actual experimental conditions, such as a specific drug substance / product, environment, personnel, equipment. The laboratory must perform method verification on already validated method during the analytical transfer, before using that method in routine analysis. In other words, method verification is required if the manufacturer of the pharmaceutical product provides an authorized validated analytical method. The laboratory needs to perform method verification to ensure that proposed method by the manufacturer can be applied in their laboratory.

Verification of the method is not performed on all parameters mentioned above, according to ICH Q2R1. The parameters that are recommended to be tested during method verification are: specificity, precision, linearity, detection limit and quantification limit.

Difference Between Analytical Method Verification and Analytical Method Validation:

From a regulatory perspective, method validation evaluates the performance of an established method through performing various analytical parameters to prove that the method is suitable for its purpose. Method verification applies the necessary analytical performance characteristics to obtain reliable data for specific types of samples, environment, or equipment during laboratory method transfer, in order not to repeat the whole validation process.

Conclusion

Method validation and method verification are required under different situations. Method validation is applied to an "new method" developed by a manufacturer of the pharmaceutical product; while method verification is applied to a "previously validated method" before it's used in a particular laboratory for the first time for routine analysis. Whenever regulatory approval is required for a pharmaceutical product, a key component of that approval is to have appropriate analytical testing procedures that must meet certain standards to ensure the safety and efficacy of the product. It is very important to distinguish when one method needs to be validated or verified and which statistical tests are appropriate for each.

References

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