RISK MANAGMENT IN THE VALIDATION OF ANALYTICAL METHODS

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Quantitative analytical methods play a central role in all activities of the pharmaceutical industry. Indeed, it is on the results obtained from analytical laboratories that are taken all the critical decisions such as batch release of a drug product, establishment and verification of shelf life, pharmacokinetic studies, and so on. The reliability of these decisions depends obviously on the quality of the results provided by these methods. Furthermore, an increasing focus is actually made on the analysis, understanding and prediction of the statistical risks associated with these measurement results. Therefore, it is crucial to know and manage these risks during the method validation phase which is the first step of the life cycle of any quantitative analytical method. It is also important to keep in mind that the objective of any analytical method is to be able to quantify as accurately as possible each of the unknown quantities that the laboratory will have to determine.

In this context, a recently methodology consists in using accuracy profiles based on β-expectation tolerance intervals for the total measurement error (including both bias and standard deviation) of validation samples and on acceptance limits fixed a priori. Such an approach allows evaluating the proportion of expected measurements inside these limits. The accuracy profile is a simple and visual decision tool allowing to evaluate the ability of the method to quantify while controlling the risks to obtain results Out Of Specification (OOS) in routine analysis. Examples illustrating the usefulness as well as the predictive character of the accuracy profile in the validation phase will be presented. Using the proposed approach, each analyst can predict the quality of the results that he will provide and thus earn confidence in the subsequent critical decisions made.

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