Step-by-Step Analytical Methods Validation and Protocol in the Quality System Compliance Industry

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Introduction

Methods Validation: Establishing documented evidence that provides a high degree of assurance that a specific method, and the ancillary instruments included in the method, will consistently yield results that accurately reflect the quality characteristics of the product tested.

Method validation is an important requirement for any package of information submitted to international regulatory agencies in support of new product marketing or clinical trials applications. Analytical methods should be validated, including methods published in the relevant pharmacopoeia or other recognized standard references. The suitability of all test methods used should always be verified under the actual conditions of use and should be well documented.

Methods should be validated to include consideration of characteristics included in the International Conference on Harmonization (ICH) guidlines[1,2] addressing the validation of analytical methods. Analytical methods outside the scope of the ICH guidance should always be validated.

ICH is concerned with harmonization of technical requirements for the registration of products among the three major geographical markets of the European Community (EC), Japan, and the United States (U.S.) of America. The recent U.S. Food and Drug Administration (FDA) methods validation guidance document,[3-5] as well as the United States Pharmacopoeia (USP),[6] both refer to ICH guidelines.

The most widely applied typical validation characteristics for various types of tests are accuracy, precision (repeatability and intermediate precision), specificity, detection limit, quantitation limit, linearity, range, and robustness *(Figure 1)*. In addition, methods validation information should also include stability of analytical solutions and system suitability.[7]

Health Canada (HC) has also issued guidance on methods validation entitled *Acceptable Methods Guidance*.[8] HC has been an observer of ICH, and has adopted ICH guidelines subsequent to its reaching Step Four of the ICH process. An acceptable method predates ICH, and HC plans to revise this guidance to reflect current ICH terminology.

Figure 2 shows the data required for different types of analysis for method validation. Where areas of the *Acceptable Methods Guidance* are superseded by ICH Guidelines Q2A[1] and Q2B,[2] HC accepts the requirements of either the ICH or *Acceptable Methods Guidance*; however, for method validation, ICH acceptance criteria are preferred. HC's *Acceptable Methods Guidance* provides useful guidance on methods not covered by the ICH guidelines (e.g., dissolution, biological methods), and provides acceptance criteria for validation parameters and system suitability tests for all methods.

HC has also issued templates recommended as an approach for summarizing analytical methods and validation data ICH terminology was used when developing these templates.

This paper suggests one technique of validating methods. There are numerous other ways to validate methods, all