Technical Report No. 57-2

Analytical Method Development and Qualification for Biotechnology Products

PDA Analytical Method Development and Qualification of Biotechnology Products Technical Report Team

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ISBN: 978-0-939459-74-2

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1.0 Introduction

This technical report provides practical, risk-based guidance for the development and qualification portions of the analytical method lifecycle for biotechnology products. It is a companion report to PDA *Technical Report No. 57: Analytical Method Validation and Transfer for Biotechnology Products.*

Method development begins with defining the requirements for the analytical method. Based on the intended use and related requirements of the method, an analytical platform is selected in concert with the appropriate materials and equipment. A method is defined through method optimization, with consideration of the final requirements of the method (e.g., sensitivity and specificity). The development of a method typically leads to, but does not necessarily finish with, its qualification, which is a documented assessment of method performance ***(1).*** This process is one means to help ensure that the method is scientifically sound (specific, sensitive, accurate, and reproducible) and is suitable and reliable for the specified purpose ***(2-4).*** Method performance may also be assessed by other means, including trending of assay controls during routine method use.

The development process depends on the use of appropriately detailed documents that describe the analytical method. Operational and maintenance procedures for equipment should be available to ensure proper functioning with respect to the intended use and phase of product development ***(4-7).***

Analytical method development (AMD) and analytical method qualification (AMQ) are typically iterative processes whereby the method is optimized, tested for its suitability (i.e., ability to meet target criteria for performance characteristics, such as precision and accuracy) through qualification studies, and potentially further optimized based on the qualification results.

The analytical target profile (ATP) is discussed in further detail in the body of this technical report as a potential means to manage AMD and AMQ. The ATP is comprised of the concepts of intended use, expected performance; measured critical quality attributes (CQAs), identified critical performance parameters, and completed iterative performance assessments. It can, therefore, be considered the structural framework for the method development and qualification process as well as for the rest of the method lifecycle continuum, including validation and routine use ***(8).***

Qualification of an analytical method typically proceeds in a phase-appropriate manner commensurate with the intended use of the method. In other words, a more extensive evaluation of method performance or qualification may be performed to support a Phase II clinical study than was used for a Phase I study, with both qualification activities being broadly based on the elements of ICH Q2(R1) guidance ***(6).*** The phase-appropriate guidance documents describe the qualification and validation activities recommended for release and stability methods in support of a particular clinical phase ***(2,3).*** For other methods, such as characterization methods, qualification can be the end goal in the method lifecycle. Formal method qualification is not a regulatory requirement prior to method validation, but it offers one means of ensuring method suitability and ability to satisfy the defined requirements (e.g., in the ATP) and to support a successful validation.

The intended use of analytical methods may change during the product development process and may affect the ATP, method requirements, and method performance expectations. AMQ provides an option to ensure the suitability of a method's use for the release of early-phase or midphase clinical trial material without generating formal and prospective analytical method validation (AMV) studies.

1.1 Method Lifecycle

The method lifecycle is the time from identification of the need for an analytical method through method retirement, including periodic reassessments of and updates to the method. This lifecycle is tied to the product lifecycle in that the status of the method must be assessed in the context of whether the product is in the early stages of clinical development or is commercially approved. An important part of the method lifecycle is to ensure that at each stage, the method is assessed and found ready to proceed to the next step. A schematic of the development and qualification elements of the lifecycle, which are detailed within this report, is provided in **Figure 1.1-1,** which also shows the link to validation, as detailed within PDA *Technical Report No. 57*.

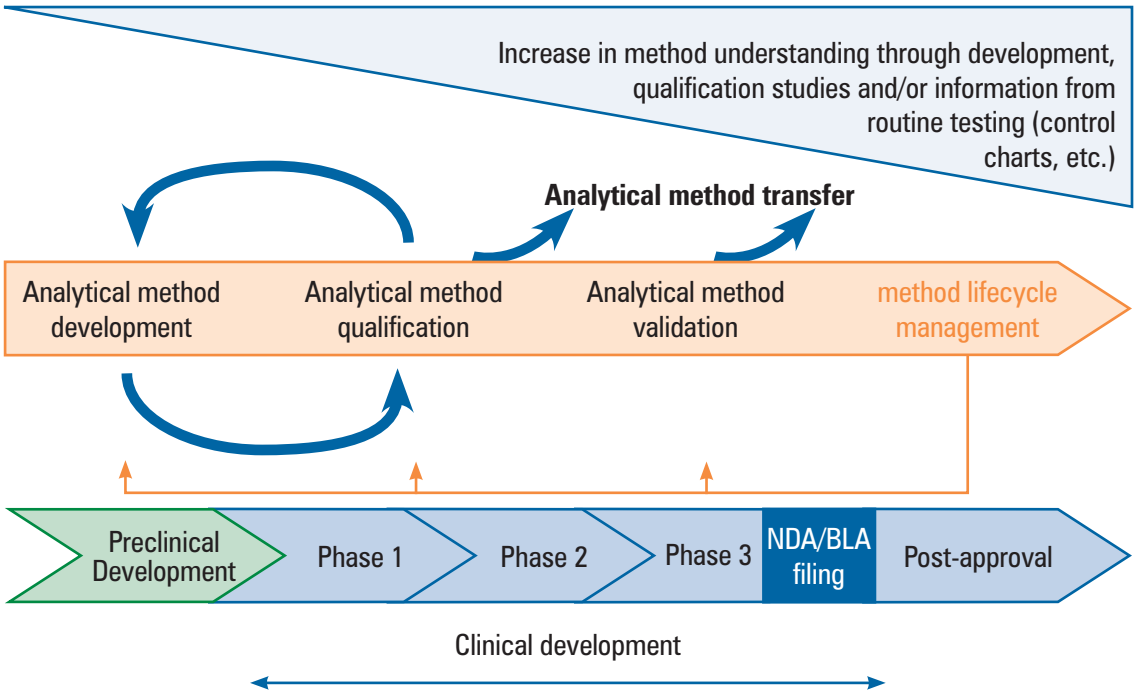

Figure 1.1-1 Method Lifecycle and its Links to Product Development

1.2 Purpose and Scope

This technical report covers method development and qualification for biotechnology products.

The content that follows describes the method development and qualification portions of the lifecycle that often lead to method validation, which is outlined in PDA *Technical Report No. 57: Analytical Method Validation and Transfer for Biotechnology Products* and ICH Q2(R1) ***(6,9).*** This report also delineates the commonalities and differences between qualification and validation, the various models for execution of qualification, and which of these models comprise the best practices of industry. The document further recognizes that terms such as "qualification" may be commensurate with phase-appropriate validation within certain company systems and regulatory environments ***(1)***. This report includes guidance for AMD and AMQ studies, such as risk-based strategies and priorities; ATP and quality-by-design (QbD) concepts; target performance criteria; and modern quality expectations, such as those presented in ICH Q8-10 guidelines ***(10-12).***

