Technical Report No. 57

Analytical Method Validation and Transfer for Biotechnology Products

2012

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PDA Analytical Method Validation And Transfer For Biotechnology Products Task Force Members

Authors

Stephan O. Krause, Ph.D., Chair, MedImmune

Florence Baudoux, Ph.D., GlaxoSmithKline

Pierre Douette, Ph.D., Eurogentec S.A.

Nicole Gibelin, Ph.D., Sanofi Pasteur, France

Alice E. Grebanier, Ph.D., Centocor R&D

Rajesh Krishnamurthy, Ph.D., Zyngenia, Inc.

Carl-Gustav, Millinger, Ph.D., Swedish Orphan Biovitrum

Frank Moffatt, Ph.D., Solvias AG

Dwayne Neal, SAIC-Frederick, Inc.

Phillip Ramsey, SAIC-Frederick, Inc.

Michael Rooney, Ph.D., BioTechLogic

Melissa J. Smith, MJ Quality Solutions

Michael Warncke, Ph.D., Bayer HealthCare

Earl K. Zablackis, Ph.D., Sanofi Pasteur, USA

Contributors

Patricia W. Cash, Ph.D., MedImmune

Larissa Chirkova, Novozymes

Marta Germano, Pharming Technologies

Siegfried Giess, Ph.D., Paul-Ehrlich Institute

Rashmi Rawat, Ph.D., U.S. FDA

The content and views expressed in this Technical Report are the result of a consensus achieved by the authorizing Task Force and are not necessarily views of the organizations they represent.

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ISBN: 978-0-939459-41-4

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1.0 Introduction

This Technical Report (TR) provides risk-based guidance for Analytical Method Validation (AMV), which follows Analytical Method Development (AMD) or Analytical Method Qualification (AMQ), and contains risk-based guidance for other, related method lifecyle steps, such as Analytical Method Transfer (AMT).

The guidance provided here builds upon the International Conference on Harmonization (ICH) Q2 (R1) guidelines and includes additional considerations for analytical platform technology (APT) methods as well as the impact of stakeholder considerations, and essentially all modern quality expectations as recommended in the ICH Q8 (R2), Q9, and Q10 guidelines ***(1–4).***

Similar to the manufacturing process, an analytical method can also be considered to be a process. The validation strategy for analytical methods could therefore conceptually follow those of Process Validation ***(5).*** AMV can then be defined as the collection and evaluation of data, from the analytical method development stage throughout routine QC testing, which establishes scientific evidence that an analytical method is capable of consistently delivering accurate and reliable results.

1.1 Scope and Purpose

This TR is to provide practical and strategic guidance to efficiently use historical data and knowledge to design suitable risk-based AMV studies, and set appropriate protocol acceptance criteria. The typical method lifecycle steps prior, during, and beyond the AMV studies are illustrated in **Figure 1.1-1**. The typical steps prior to validation, usually performed at early pharmaceutical development stages, are included in this figure to show the dependency among early- and late-stage lifecycle steps. The AMV process begins with the validation readiness assessment and continues with the post-validation steps, maintenance (validation continuum), transfer(s), comparability, as they may apply to the continuous demonstration of analytical method suitability. The typical sequence of all prevalidation, validation and post-validation steps, as illustrated in the bottom half of **Figure 1.1-1,** is reflected in the sequence of sections in this TR. Instead of dealing in great detail with many possible exceptions and special considerations, this TR is intended to provide practical guidance to typical development processes and AMV studies.

The guidance presented in this TR applies to all biotechnological manufacturers and all contract development and manufacturing organizations. This TR does not provide specific guidance for the timing of AMV study execution with respect to the parallel product development lifecycle stages or guidance for analytical instrument qualification.

It should be considered that various new analytical technologies and/or the use of Process Analytical Technology (PAT) methods may suggest some modification to the validation strategies presented here. Specific aspects for the validation of bioassays such as curve fitting models and statistical reference-to-sample parallelism requirements are not covered in this TR. Case-specific considerations for microbiological method validation such as statistical sampling and testing environment conditions are also not covered as they depend on the analytical methodology and the intended use.

AMV studies are typically executed for future routine-use methods but may not be required for analytical methods used in support of pharmaceutical development ***(5).*** **Figure 1.1-2** illustrates the two different analytical method lifecycle paths separated according to the intended use of a particular method. The intended use of a particular method can be assessed early as part of the overall quality target product profile (QTPP) and a method should be selected accordingly. The intended use should be further considered when developing, qualifying and validating analytical methods. For example, measuring a critical quality attribute (CQA) or a critical process parameter (CPP) may require a more rigorous approach to the overall validation process. The intended use of a method can change during the method and/or product lifecycle(s) due to a specification change or other reasons.