



Standard Guide for Risk-Based Validation of Analytical Methods for PAT Applications¹

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1. Scope

1.1 This guide provides an overview to the risk-based validation of process analytical methods under a process analytical technology (PAT) paradigm for pharmaceuticals and biopharmaceuticals and as such includes guidance on assessing risk to product quality from inappropriate method validation.

1.2 This guide builds on existing standards on the topic of validation concentrating on applying such standards to analytical methods for on-line analysis. In particular, it addresses the validation of at-line, on-line, or in-line PAT measurements and covers both API and Drug Product (DP) measurements.

1.3 The definitions of International Conference on Harmonization (ICH) validation parameters (such as specificity, precision, repeatability, etc.) apply; however, the method of demonstrating the validation parameters may vary from that described in ICH and is discussed.

1.4 As consistent with the U.S. Food and Drug Administration (FDA) process validation guidance, this document also briefly covers ongoing assurance that the method remains in a validated state during routine use.

1.5 Equipment and instrument qualification are out of the scope of this guide but will be referenced as inputs to validation of analytical methods for PAT applications.

1.6 The validation of multivariate prediction models is out of scope but will be referenced as inputs to validation of analytical methods for PAT applications.

1.7 Microbiological methods are out of scope.

1.8 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and determine the applicability of regulatory limitations prior to use.*

¹ This guide is under the jurisdiction of ASTM Committee E55 on Manufacture of Pharmaceutical Products and is the direct responsibility of Subcommittee E55.01 on PAT System Management, Implementation and Practice.

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2. Referenced Documents

2.1 ASTM Standards:²

D3764 Practice for Validation of the Performance of Process Stream Analyzer Systems

D6122 Practice for Validation of the Performance of Multivariate Online, At-Line, and Laboratory Infrared Spectrophotometer Based Analyzer Systems

E1655 Practices for Infrared Multivariate Quantitative Analysis

E1790 Practice for Near Infrared Qualitative Analysis

E2056 Practice for Qualifying Spectrometers and Spectrophotometers for Use in Multivariate Analyses, Calibrated Using Surrogate Mixtures

E2476 Guide for Risk Assessment and Risk Control as it Impacts the Design, Development, and Operation of PAT Processes for Pharmaceutical Manufacture

E2500 Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment

E2617 Practice for Validation of Empirically Derived Multivariate Calibrations

E2629 Guide for Verification of Process Analytical Technology (PAT) Enabled Control Systems

E2656 Practice for Real-time Release Testing of Pharmaceutical Water for the Total Organic Carbon Attribute

2.2 ICH Standards:³

Q2(R1) Guidance on Validation of Analytical Procedures: Text and Methodology

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients

Q9 Quality Risk

ICH Quality Implementation Working Group Points to Consider (R2) ICH-Endorsed Guide for ICH Q8/Q9/Q10 Implementation dated 6 December 2011

² For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at service@astm.org. For *Annual Book of ASTM Standards* volume information, refer to the standard's Document Summary page on the ASTM website.

³ Available from International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), ICH Secretariat, c/o IFPMA, 15 ch. Louis-Dunant, P.O. Box 195, 1211 Geneva 20, Switzerland, <http://www.ich.org>.