



Standard Guide for Multivariate Data Analysis in Pharmaceutical Development and Manufacturing Applications¹

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1. Scope

1.1 This guide covers the applications of multivariate data analysis (MVDA) to support pharmaceutical development and manufacturing activities. MVDA is one of the key enablers for process understanding and decision making in pharmaceutical development, and for the release of intermediate and final products.

1.2 The scope of this guide is to provide general guidelines on the application of MVDA in the pharmaceutical industry. While MVDA refers to typical empirical data analysis, the scope is limited to providing a high level guidance and not intended to provide application-specific data analysis procedures. This guide provides considerations on the following aspects:

1.2.1 Use of a risk-based approach (understanding the objective requirements and assessing the fit-for-use status),

1.2.2 Considerations on the data collection and diagnostics used for MVDA (including data preprocessing and outliers),

1.2.3 Considerations on the different types of data analysis and model validation,

1.2.4 Qualified and competent personnel, and

1.2.5 Life-cycle management of MVDA.

1.3 *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.*

2. Referenced Documents

2.1 ASTM Standards:²

C1174 Practice for Prediction of the Long-Term Behavior of Materials, Including Waste Forms, Used in Engineered

Barrier Systems (EBS) for Geological Disposal of High-Level Radioactive Waste

E178 Practice for Dealing With Outlying Observations

E1355 Guide for Evaluating the Predictive Capability of Deterministic Fire Models

E1655 Practices for Infrared Multivariate Quantitative Analysis

E1790 Practice for Near Infrared Qualitative Analysis

E2363 Terminology Relating to Process Analytical Technology in the Pharmaceutical Industry

E2474 Practice for Pharmaceutical Process Design Utilizing Process Analytical Technology

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

E2617 Practice for Validation of Empirically Derived Multivariate Calibrations

2.2 ICH Standards:³

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

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

3. Terminology

3.1 *Definitions*—Common term definitions can be found in Terminology **E2363** for pharmaceutical applications and some terms can be found in other standards and are cited when they are mentioned.

4. Significance and Use

4.1 A significant amount of data is being generated during pharmaceutical development and manufacturing activities. The interpretation of such data is becoming increasingly difficult. Individual examination of the univariate process variables is relevant but can be significantly complemented by multivariate data analysis (MVDA). Such methodology has been shown to be particularly efficient at handling large amounts of data from

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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>.