



Standard Guide for Application of Continuous Processing in the Pharmaceutical Industry¹

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1. Scope

1.1 This guide introduces key concepts and principles to assist in the appropriate selection, development and operation of continuous processing technologies for the manufacture of pharmaceutical products.

1.2 Particular consideration is given to the development and application of the appropriate scientific understanding and engineering principles that differentiate continuous manufacture from traditional batch manufacturing.

1.3 Most of the underlying concepts and principles (for example, process dynamics and process control) outlined in this guide can be applied in both Drug Substance (DS) and Drug Product (DP) processes. However it should be recognized that in Drug Substance production the emphasis may be more on chemical behavior and dynamics in a fluid phase whereas for drug product manufacture there may be a greater emphasis on the physical behavior and dynamics in a solid/powder format.

1.4 This guide is also intended to apply in both the development of a new process, or the improvement/redesign of an existing one.

1.5 The values stated in SI units are to be regarded as standard. No other units of measurement are included in this standard.

1.6 *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 Process Understanding and PAT System Management, Implementation and Practice.

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2. Referenced Documents

2.1 ASTM Standards:²

E2363 Terminology Relating to Process Analytical Technology in the Pharmaceutical Industry

E2475 Guide for Process Understanding Related to Pharmaceutical Manufacture and Control

E2537 Guide for Application of Continuous Quality Verification to Pharmaceutical and Biopharmaceutical Manufacturing

E2898 Guide for Risk-Based Validation of Analytical Methods for PAT Applications

2.2 FDA Documents:³

FDA Guidance for Industry PAT A Framework for Innovative Pharmaceutical Development, Manufacturing, and Quality Assurance (2004)

3. Terminology

3.1 Definitions:

3.1.1 For general definitions, refer to Terminology E2363 and Guides E2537 and E2475.

3.2 Definitions of Terms Specific to This Standard:

3.2.1 *back mixed process*—a process with a residence time distribution (RTD) which is non zero and potentially significant compared to the mean residence time.

3.2.1.1 *Discussion*—For example, in an idealized fully back mixed process quantities of material will be mixed into a single homogeneous condition such that a rapid step change in the properties of inlet material will not result in an equivalent step change in the properties of the output material but will be reflected in a more gradual change. The rate of this change will depend on the equipment characteristics, residence volume,

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 Food and Drug Administration (FDA), 10903 New Hampshire Ave., Silver Spring, MD 20993-0002, <http://www.fda.gov>.