



Standard Practice for Real-time Release Testing of Pharmaceutical Water for the Total Organic Carbon Attribute¹

This standard is issued under the fixed designation E2656; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ϵ) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 This practice establishes an approach to the real-time release testing (RTRT) of pharmaceutical water based on the total organic carbon (TOC) attribute using on-line total organic carbon (OLTOC) instrumentation that is in agreement with current regulatory thinking.

1.2 This practice is harmonized with or supports the concepts of relevant ASTM International Committee E55 on Manufacture of Pharmaceutical Products standards, ICH Harmonized Tripartite Guidelines, the U.S. FDA PAT Guidance, and U.S. FDA Pharmaceutical cGMPs.

1.3 This practice does not provide general guidance information for pharmaceutical procedures that are considered standard practice in the pharmaceutical industry. This practice provides specific guidance for non-standardized procedures.

1.4 This practice does not address the user's various internal procedures for risk, change, or quality management systems. The overall project effort associated with this practice shall be proportional to the overall risk of failing the pharmaceutical water's TOC concentration specification.

1.5 This practice does not purport to establish how to comply with pharmacopeias. The RTRT methodology selected must assure compliance with the user's current required pharmacopeias. However, compliance with pharmacopeia TOC methods is not necessarily sufficient to meet current regulatory expectations for RTRT.

1.6 This practice does not purport to substitute for or replace compendial bioburden testing requirements. It is strictly applicable to the TOC attribute of water quality.

1.7 *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 practice is under the jurisdiction of ASTM Committee E55 on Manufacture of Pharmaceutical and Biopharmaceutical Products and is the direct responsibility of Subcommittee E55.03 on General Pharmaceutical Standards.

Current edition approved Nov. 1, 2016. Published November 2016. Originally approved in 2010. Last previous edition approved in 2010 as E2656 – 10. DOI: 10.1520/E2656-16.

2. Referenced Documents

2.1 ASTM Standards:²

E2281 Practice for Process Capability and Performance Measurement

E2363 Terminology Relating to Process Analytical Technology in the Pharmaceutical Industry

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

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

D4839 Test Method for Total Carbon and Organic Carbon in Water by Ultraviolet, or Persulfate Oxidation, or Both, and Infrared Detection

D5173 Guide for On-Line Monitoring of Total Organic Carbon in Water by Oxidation and Detection of Resulting Carbon Dioxide

D5904 Test Method for Total Carbon, Inorganic Carbon, and Organic Carbon in Water by Ultraviolet, Persulfate Oxidation, and Membrane Conductivity Detection

D5997 Test Method for On-Line Monitoring of Total Carbon, Inorganic Carbon in Water by Ultraviolet, Persulfate Oxidation, and Membrane Conductivity Detection

D6317 Test Method for Low Level Determination of Total Carbon, Inorganic Carbon and Organic Carbon in Water by Ultraviolet, Persulfate Oxidation, and Membrane Conductivity Detection

2.2 Pharmacopoeia Documents:

ICH Q2 (R1) Validation of Analytical Procedures: Text and Methodology³

ICH Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients³

ICH Q8 (R2) Pharmaceutical Development³

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>.