



Standard Guide for Testing Absorbable Stents¹

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1. Scope

1.1 This Guide covers select physical and mechanical characterizations of vascular stents with one or more absorbable components. Such absorbable stents (also referred to as vascular scaffolds) are used to provide temporary luminal support of the coronary and peripheral vasculature following interventional revascularization procedures. This Guide covers devices that are fabricated from one or more degradable polymers and/or metals (from this point on referred to as “absorbable”). This Guide provides a framework for evaluating the change in select physical and mechanical characteristics of absorbable stents from manufacture through their intended degradation *in vivo*. Specific testing recommendations are limited to existing ASTM standards for stent evaluation.

1.2 Recommendations specific to non-absorbable stents with absorbable coatings are not within scope.

1.3 Recommendations specific to testing absorbable stent grafts are not provided here, however this standard has many elements applicable to testing absorbable stent grafts.

1.4 Clinical need dictates that absorbable stents initially possess the same general dimensions and mechanical function as their non-absorbable counterparts. Thus, utilization of already established mechanical stent evaluation methods is possible when absorbable test specimens are previously conditioned under physiologically relevant temperature and humidity. As a result, this standard addresses absorbable-specific testing issues related to the mechanical and physical evaluation of these devices. This standard is limited to providing absorbable-specific testing recommendations for evaluations where an ASTM method for durable (i.e., non-absorbable) stents is already available. Specifically, this standard provides testing recommendations for adapting the elastic recoil (ASTM F2079), securement/dislodgement (ASTM F2394), and three-point bending (ASTM F2606) tests to fully absorbable devices. This guide generally describes specimen conditioning, as appropriate, for absorbable devices, which can range from none to extensive – depending on the measured attribute and

relevant clinical exposure conditions, including time in the in-use environment. There are additional stent evaluation methods that are not addressed explicitly in this guide, e.g., chronic durability, that may require absorbable-specific provisions. The user should justify the appropriate testing for the specific polymer and device.

1.4.1 While the primary purpose of this guide is to address absorbable stent-related issues specific to the tests described in Section 1.3, additional testing (e.g., radial strength) will likely also be needed. Thus, aspects of what is presented herein may be applicable to additional relevant device attributes, such as those described in ISO 25539-1 and/or 25539-2.

1.5 This Guide may not be appropriate for all absorbable devices, for example those that possess limited hydrolytic or corrosion susceptibility and degrade *in vivo* primarily through enzymatic action. The user is cautioned to consider the appropriateness of the standard in view of the particular absorbable device and its potential application.

1.6 This Guide does not address the methods necessary to characterize the chemical degradation of the absorbable stent (e.g., changes in mass, molecular weight, or degradants). However, this type of characterization does represent an important component of the degradation profile and mechanism of the device. These characterizations are addressed in ASTM F1635.

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

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.*

2. Referenced Documents

2.1 ASTM Standards:²

D618 Practice for Conditioning Plastics for Testing
E6 Terminology Relating to Methods of Mechanical Testing

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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.

- E122 Practice for Calculating Sample Size to Estimate, With Specified Precision, the Average for a Characteristic of a Lot or Process
- E1823 Terminology Relating to Fatigue and Fracture Testing
- F1635 Test Method for *in vitro* Degradation Testing of Hydrolytically Degradable Polymer Resins and Fabricated Forms for Surgical Implants
- F2079 Test Method for Measuring Intrinsic Elastic Recoil of Balloon-Expandable Stents
- F2394 Guide for Measuring Securement of Balloon Expandable Vascular Stent Mounted on Delivery System
- F2477 Test Methods for *in vitro* Pulsatile Durability Testing of Vascular Stents
- F2606 Guide for Three-Point Bending of Balloon Expandable Vascular Stents and Stent Systems
- F2914 Guide for Identification of Shelf-life Test Attributes for Endovascular Devices

2.2 Other Standards:³

- ISO 14630 Non-Active Surgical Implants—General Requirements
- ISO 25539-1 Cardiovascular implants—Endovascular devices—Part 1: Endovascular prostheses
- ISO 25539-2 Cardiovascular implants—Endovascular devices—Part 2: Vascular stents
- ISO 10993-1 Biological evaluation of medical devices—Part 1: Evaluation and testing within a risk management process
- ISO 10993-9 Biological evaluation of medical devices—Part 9: Framework for identification and quantification of potential degradation products
- ISO 10993-13 Biological evaluation of medical devices—Part 13: Identification and quantification of degradation products from polymeric medical device
- ISO 10993-15 Biological evaluation of medical devices—Part 15: Identification and quantification of degradation products from metals and alloys

3. Terminology

3.1 Definitions:

3.1.1 Unless otherwise defined in this standard, the terminology related to mechanical testing that is used in these test methods will be in accordance with the definitions of Terminologies ASTM E6 and ASTM E1823, and the respective standards described in the annexes of this document.

3.1.2 *absorbable, adj*—in the body, referring to an initially distinct foreign material or substance that either directly or through intended degradation can be excreted, metabolized or assimilated by cells and/or tissue.

3.1.3 *stent, vascular, n*—a structure implanted in the native or grafted vasculature that is intended to provide mechanical radial support to enhance vessel patency.

3.1.4 *conditioning, v*—preparation of the device prior to mechanical testing to include elements that (1) affect the

attribute to be tested, and (2) are imposed on device per clinical and/or degradation timeline up to points of interest for the attribute.

4. Significance and Use

4.1 Absorbable cardiovascular stents provide temporary support to the vasculature and are intended to degrade and absorb over time after being implanted into the vasculature.

4.2 The test methods used to evaluate the mechanical performance of absorbable devices are similar to those used to evaluate permanent (non-absorbable) cardiovascular devices. The absorbable-specific pre-test conditioning requirements, handling requirements before and during the test, and time-dependent mechanical property evaluations for absorbable devices are addressed here.

4.3 As the absorbable implant degrades, the mechanical performance of the device also deteriorates. The key to achieving effective revascularization with absorbable devices is to provide an adequate level of luminal support for the time frame needed for vessel stabilization.

5. Materials and Manufacture

5.1 The manufacturer should ensure that materials used to manufacture absorbable implants are suitable for implanting into the body. General requirements regarding a material's suitability for use as an implant are described in ISO 14630. Methods and guidance for assessment of biocompatibility can be found in ISO 10993. There may be additional issues related to the biocompatibility of absorbable materials that are not covered in ISO 10993.

6. General Requirements and Performance Considerations

6.1 *Absorbable Stents*—The following considerations may be important when determining the suitability of a stent for a particular application. However, the test methods referenced as in the Annexes may not be appropriate for all types of implant applications. The user is cautioned to consider the appropriateness of the test methods in view of the devices being tested and their potential application.

6.1.1 Performance Considerations:

6.1.1.1 To better characterize the degradation and degradation products of the absorbable stent, significant effort should be undertaken toward developing an *in vitro* model for the anticipated *in vivo* degradation mechanism (e.g., corrosion, hydrolysis, etc.). Such a model would reflect the implant's composition and any related interaction(s) with the physiologically relevant aqueous solution, including – as appropriate – consideration of the influence of additives (e.g., antimicrobials), temperature, ionic composition and strength, pH, and fluid flow conditions. This *in vitro* model might also be used to assess subsequent changes to the absorbable stent in lieu of animal experimentation.

6.1.1.2 Composition/chemical properties in the finished, sterilized state and during degradation.

6.1.1.3 Mechanical behavior of the finished, sterilized device and during degradation. Mechanical evaluation should be completed for relevant device attributes including, but not

³ Available from American National Standards Institute (ANSI), 25 W. 43rd St., 4th Floor, New York, NY 10036, <http://www.ansi.org>.

limited to bending (e.g., bending stiffness). Additional mechanical characteristics may need to be evaluated to determine the degree of vascular support and resistance to non-radial vessel deformation.

6.1.1.4 While chronic durability should be assessed for absorbable stents, this Guide does not specify methods to perform this characterization. The user should justify the appropriate durability testing for the specific absorbable stent, including structural integrity and the potential for device embolization.

6.1.2 *Aging and Shelf Life Requirements:*

6.1.2.1 The user should establish the labeled shelf-life of the absorbable device through appropriate real-time studies according to ASTM F2914. A justification for attributes covered in this guide not addressed as part of real-time studies should be provided. Accelerated testing may be performed with appropriate justification.

7. General Sampling, Conditioning, and Testing Considerations

7.1 *Apparatus, Equipment, and Materials*—The test equipment should be maintained to the necessary precision and accuracy, as appropriate for the specific device and functional output being tested.

7.1.1 *Specimen Container*—A glass or plastic container capable of holding the test specimen and the conditioning solution should be used. The container should be sealable to prevent solution loss due to evaporation, as appropriate. Multiple specimens may be stored in the same container, provided (1) suitable specimen separation is maintained to allow fluid access to each specimen surface (2) specimen-to-specimen contact is precluded, and (3) the environment is identical.

7.1.2 *Conditioning/Soaking Solution:*

7.1.2.1 For absorbable stents manufactured from hydrolytically degradable polymers, a physiologically relevant aqueous solution should be used. (For more detail see ASTM F1635 and References contained in Section X1.2)

7.1.2.2 For absorbable stents fabricated from degradable (corrodible) metals, a physiologically relevant aqueous solution with appropriate pH, buffer capacity, isotonicity, and ion concentration should be used (e.g., artificial plasma: ISO 10993-15). The user is cautioned that the ions present in the soaking solution (and in blood) may carry potential to chemically react with the released metallic ions.

7.1.2.3 If accelerated degradation is desired, changes in temperature, pH, or composition of solution may be used with appropriate justification.

7.1.3 *Constant Temperature Bath or Oven:*

7.1.3.1 An aqueous bath or oven capable of maintaining the specimens at a physiologic temperature ($37 \pm 2^\circ\text{C}$) for the specified testing periods should be used.

7.1.3.2 The fluid environment should be well-mixed during conditioning and mechanical testing.

7.1.4 *pH Meter:*

7.1.4.1 A pH metering device with appropriate accuracy and precision in the physiological range (pH 6 to pH 8) should be used.

7.2 *Specimen Acquisition & Evaluation Frequency:*

7.2.1 *Sampling*—If appropriate, representative random specimens should be taken from multiple batches/lots in accordance with Practice E122.

7.2.2 *Evaluation Frequency*—For a complete history of the behavior of a specimen during degradation and absorption, functional attributes of the device should be evaluated at appropriate time points determined by resolution required to confidently characterize the decline in mechanical properties of the device and the time frame over which the attribute are relevant.

7.2.2.1 Evaluation time points should be both clinically relevant and reflective of the expected changes resulting from exposure to the physiologically relevant aqueous solution (e.g., degradation).

7.2.2.2 The testing intervals should be documented in the test report.

7.3 *Conditioning*—All devices subjected to conditioning should be completely fabricated, and finished absorbable stents or stent systems should be sterilized as intended by the manufacturer. This section provides guidance for characterization of the performance of the stent over time, with sufficient resolution to adequately characterize the attribute.

7.3.1 Fig. 1 presents a timeline for the sterilized, finished, absorbable device in different environments and conditions; however, the durations of each phase will vary depending on the device material and design.

7.3.1.1 The conditioning performed prior to evaluation of a specific attribute should include all relevant exposures up to the final time point for the attribute (see 7.3.2). Relevant exposures may include humidity, flow, radial and non-radial cyclic deformation, all of which need to be conducted under relevant thermal conditions.

7.3.1.2 It may be necessary to measure additional functional attributes of the device as dictated by the indications for use and/or failure mode.

7.3.2 Upon introduction to the physiologically relevant aqueous solution, polymeric absorbable materials will uptake fluid prior to hydrolysis, which may affect some attributes. For example, stent radial strength may increase with fluid uptake prior to a significant change in molecular weight. The user should consider characterizing these dynamic attributes upon deployment of the device and during hydration, prior to a significant decline in molecular weight. Such attributes should also be monitored at multiple time points throughout degradation in order to characterize their change over time.

7.3.2.1 If the time frame for fluid uptake is very short, it may not be possible to measure some device functional attributes after stable hydration and before onset of degradation. In these instances, evaluation of device functional attributes at deployment as well as interim points at multiple time points during degradation may be adequate.

7.3.2.2 The time required for the specimen to reach a stable temperature and/or hydration state may extend longer than the time frame for a particular attribute to become clinically relevant. For example, stent securement is only relevant from insertion through deployment (or through withdrawal if assessing withdrawal repositioning, or aborted (retrieval) attempts;