NOTICE: This standard has either been superseded and replaced by a new version or withdrawn. Contact ASTM International (www.astm.org) for the latest information.

Designation: F 1635 – 04

Standard Test Method for *in vitro* Degradation Testing of Hydrolytically Degradable Polymer Resins and Fabricated Forms for Surgical Implants[1]

This standard is issued under the fixed designation F 1635; 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 test method covers *in vitro* degradation of hydrolytically degradable polymers (HDP) intended for use in surgical implants.

1.2 The requirements of this test method apply to HDPs in various forms:

1.2.1 Virgin polymer resins, or

1.2.2 Any form fabricated from virgin polymer such as a semi-finished component of a finished product, a finished product, which may include packaged and sterilized implants, or a specially fabricated test specimen.

1.3 This test method has no provisions for mechanical loading, fluid flow, or other dynamic challenges.

1.4 *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]

D 638 Test Method for Tensile Properties of Plastics

D 671 Test Method for Flexural Fatigue of Plastics by Constant-Amplitude-of-Force[3]

D 695 Test Method for Compressive Properties of Rigid Plastics

D 747 Test Method for Apparent Bending Modulus of Plastics by Means of a Cantilever Beam

D 790 Test Method for Flexural Properties of Unreinforced and Reinforced Plastics and Electrical Insulating Materials

D 882 Test Method for Tensile Properties of Thin Plastic Sheeting

D 1708 Test Method for Tensile Properties of Plastics by Use of Microtensile Specimens

D 1822 Test Method for Tensile-Impact Energy to Break Plastics and Electrical Insulating Materials

D 2857 Test Method for Dilute Solution Viscosity of Polymers

F 748 Practice for Selecting Generic Biological Test Methods for Materials and Devices

2.2 *Other Referenced Standard:*

ISO 10993-9:1999 Biological Evaluation of Medical Devices—Part 9 Framework for Identification and Quantification of Potential Degradation Products[4]

3. Terminology

3.1 *Definitions:*

3.1.1 *resin*—any polymer that is a basic material for plastics.[5]

3.1.2 *hydrolytically degradable polymer (HDP)*—any polymeric material in which the primary mechanism of chemical degradation in the body is by hydrolysis (water reacting with the polymer resulting in cleavage of the chain).

4. Summary of Test Method

4.1 Samples of polymer resins, semi-finished components, finished surgical implants, or specially designed test specimens fabricated from those resins are placed in buffered saline solution at physiologic temperatures. Samples are periodically removed and tested for various material or mechanical properties at specified intervals. The required test intervals vary greatly depending on the specific polymeric composition. For example, poly(*l*-lactide) and poly(*e*-caprolactone) degrade very slowly and can require two or more years for complete degradation. Polymers based substantially on glycolide can completely degrade in two to three months depending on the

[1] This test method is under the jurisdiction of ASTM Committee F04 on Medical and Surgical Materials and Devices and is the direct responsibility of Subcommittee F04.15 on Material Test Methods.

Current edition approved May 1, 2004. Published June 2004. Originally approved in 1995. Last previous edition approved in 2000 as F 1635 – 95 (2000).

[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] Withdrawn.

[4] Available from American National Standards Institute (ANSI), 25 W. 43rd St., 4th Floor, New York, NY 10036.

[5] *Polymer Technology Dictionary*, Tony Whelan ed., Chapman & Hall, 1994.

Copyright © ASTM International, 100 Barr Harbor Drive, PO Box C700, West Conshohocken, PA 19428-2959, United States.

NOTICE: This standard has either been superseded and replaced by a new version or withdrawn. Contact ASTM International (www.astm.org) for the latest information.

exact composition and on the size of the specimen. Degradation time is also strongly affected by specimen size, polymer molecular weight, and crystallinity.

5. Significance and Use

5.1 This test method is intended to help assess the biodegradation rates (that is, the mass loss rate) and changes in material or structural properties, or both, of HDP materials used in surgical implants. Polymers that are known to degrade primarily by hydrolysis include but are not limited to homopolymers and copolymers of *l*-lactide, *d*-lactide, *d,l*-lactide glycolide, caprolactone, and *p*-dioxanone.[6]

5.2 This test method may not be appropriate for all types of implant applications or for all known absorbable polymers. The user is cautioned to consider the appropriateness of the test method in view of the materials being tested and their potential application (see X1.1.1).

5.3 Since it is well known that mechanical loading can increase the degradation rate of absorbable polymers, the presence and extent of such loading needs to be considered when comparing *in vitro* behavior with that expected or observed *in vivo*. Where feasible, it is recommended during degradation testing to simulate the *in vivo* loading conditions expected in the intended application. The nature and frequency of the applied mechanical load must be considered on a case by case basis, with specifics beyond the scope of this test method.

5.4 Absorbable devices subjected to flow conditions (for example, vascular stents) may degrade more rapidly than the same device maintained under static degradation test conditions. In specific cases it may be possible to predict the flow conditions that an implant will be subjected to *in vivo* and replicate them *in vitro*. However, details regarding appropriate flow modeling are beyond the scope of this test method.

5.5 Sterilization of HDP materials should be expected to cause changes in molecular weight or structure, or both, of the polymers. This can affect the initial mechanical and physical properties of a material or device, as well as its subsequent rate of degradation. Therefore, if a test is intended to be representative of actual performance *in vivo*, specimens shall be packaged and sterilized in a manner consistent with that of the final device. Non-sterilized specimens may be included for comparative purposes.

6. Materials and Apparatus

6.1 *Physiologic Soaking Solution*—A phosphate-buffered saline (PBS) solution shall be used. The pH of the solution shall be maintained at 7.4 ± 0.2 (see X1.3) unless it is determined through documented literature or self-advised study that the pH should be different due to the physiological conditions of the intended application (this may require use of an alternate buffer system). Limited excursions outside of the specified pH range are tolerable provided the time weighted average pH after buffer replenishment is maintained within this range (see X1.3.1). The ionic concentration should be in the physiological range for the intended application (for example, a solution that contains 0.1 M phosphate buffer and 0.1 M NaCl would be appropriate for most tissue or blood contact devices). The solution-to-HDP mass ratio shall be as high as practical. Although there is some experience with ratios as low as 20:1, the experimenter is cautioned that at lower ratios (that is, less buffering capacity) the solution pH may change more quickly. In accordance with 9.1.3 and X1.4, aging/testing is to be terminated if the solution temperature or pH are allowed to drift outside of the specified ranges. Higher solution/specimen ratios (for example, 100:1) will be more likely to facilitate maintenance of stable aging conditions.

6.1.1 Over the course of the study, the pH should be monitored frequently and the solution shall be changed periodically in order to maintain the pH within the acceptable limits. Refer to X1.5 for additional information.

6.1.2 Other physiologic solutions, such as bovine serum, may be substituted provided the solution is properly buffered. An anti-microbial additive should be used to inhibit the growth of microorganisms in the solution during the test period but the investigator must demonstrate through literature reference or experimentation that the chosen antimicrobial does not affect the degradation rate. Section X1.6 provides additional information. The appropriate MSDS should always be consulted concerning toxicity, safe use, and disposal of such additives.

6.2 *Sample Container*—A self-contained, inert container (bottle, jar, vial, and so forth) capable of holding the test sample and the required volume of physiologic soaking solution (see X1.7). Multiple samples may be stored in the same container provided that suitable sample separation is maintained to allow fluid access to each sample surface and to preclude sample-to-sample contact. Each container must be sealable against solution loss by evaporation.

6.3 *Constant Temperature Bath or Oven*—An aqueous bath or heated air oven capable of maintaining the samples and containers at physiologic temperatures, 37 ± 2°C, for the specified testing periods.

6.4 *pH Meter*—A pH metering device sensitive in the physiological range (pH 6 to pH 8) with a precision of 0.02 or better.

6.5 *Balance*—A calibrated weighing device capable of measuring the weight of a sample to a precision of 0.1 % of its initial weight. A balance having precision to 0.05 % or 0.01 % will facilitate establishment of an appropriate specimen drying period.

6.6 *Other*—Additional equipment as deemed appropriate by the specific test method.

7. Sampling

7.1 *Weight Loss*—A minimum of three samples shall be tested per time period.

7.2 *Molecular Weight*—A minimum of three samples shall be tested per time period.

7.3 *Mechanical Testing*—A minimum of six samples shall be tested per time period.

NOTE 1—Statistical significance may require more than the minimum number of samples to be tested.

7.4 *Solution Temperature and pH*—Soaking solutions shall be tested on a periodic basis throughout the test duration. The

[6] *Handbook of Biodegradable Polymers*, A.J. Domb ed., Harwood Academic Publishers, 1997.