Designation: F1635 – 16

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 F1635; 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 provides guidance for mechanical loading or fluid flow, or both, when relevant to the device being evaluated. The specifics of loading type, magnitude, and frequency for a given application are beyond the scope of this test method.

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

1.5 *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]

D638 Test Method for Tensile Properties of Plastics

D671 Test Method for Flexural Fatigue of Plastics by Constant-Amplitude-of-Force (Withdrawn 2002)[3]

D695 Test Method for Compressive Properties of Rigid Plastics

D747 Test Method for Apparent Bending Modulus of Plastics by Means of a Cantilever Beam

D790 Test Methods for Flexural Properties of Unreinforced and Reinforced Plastics and Electrical Insulating Materials

D882 Test Method for Tensile Properties of Thin Plastic Sheeting

D1708 Test Method for Tensile Properties of Plastics by Use of Microtensile Specimens

D1822 Test Method for Tensile-Impact Energy to Break Plastics and Electrical Insulating Materials

D2857 Practice for Dilute Solution Viscosity of Polymers

F748 Practice for Selecting Generic Biological Test Methods for Materials and Devices

2.2 *ISO Standards:*[4]

ISO 31–8 Physical Chemistry and Molecular Physics - Part 8: Quantities and Units

ISO 10993–1 Biological Evaluation of Medical Devices—Part 1 Evaluation and Testing

ISO 10993–9 Biological Evaluation of Medical Devices—Part 9 Framework for Identification and Quantification of Potential Degradation Products

ISO 13781 Poly(L-lactide) resins and fabricated forms for surgical implants – In vitro degradation testing

2.3 *NIST Standard:*[5]

NIST Special Publication SP811 Guide for the Use of the International System of Units (SI)

3. Terminology

3.1 *Definitions:*

[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.

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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] The last approved version of this historical standard is referenced on www.astm.org.

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

[5] Available from National Institute of Standards and Technology (NIST), 100 Bureau Dr., Stop 1070, Gaithersburg, MD 20899-1070, at http://physics.nist.gov/cuu/Units/bibliography.html.

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

NOTE 1—See Appendix X2 for a discussion regarding the usage of absorbable and other related terms.

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).

3.1.3 *resin*—any polymer that is a basic material for plastics.[6]

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

NOTE 2—The term molecular weight (abbreviated MW) is obsolete and should be replaced by the SI (Système Internationale) equivalent of either relative molecular mass (M_r), which reflects the dimensionless ratio of the mass of a single molecule to an atomic mass unit [see ISO 31–8], or molar mass (M), which refers to the mass of a mole of a substance and is typically expressed as grams/mole. For polymers and other macromolecules, use of the symbols M_w, M_n, and M_z continue, referring to mass-average molar mass, number-average molar mass, and z-average molar mass, respectively. For more information regarding proper utilization of SI units, see NIST Special Publication SP811.

5. Significance and Use

5.1 This test method is intended to help assess the degradation 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.[7]

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*.

5.3.1 *Mechanically Unloaded Hydrolytic Evaluation*—Conditioning of a hydrolysable device under mechanically unchallenged hydrolytic conditions at 37°C in buffered saline is a common means to obtain a first approximation of the degradation profile of an absorbable material or device. It does not necessarily represent actual *in vivo* service conditions, which can include mechanical loading in a variety of forms (for example. static tensile, cyclic tensile, shear, bending, and so forth). If the performance of a device under its indicated use includes loading, hydrolytic aging alone is NOT sufficient to fully characterize the device.

5.3.2 *Mechanically Loaded Hydrolytic Evaluation*—The objective of loading is to approximate (at 37°C in buffered saline) the actual expected device service conditions so as to better understand potential physicochemical changes that may occur. Such testing can be considered as necessary if loading can be reasonably expected under *in vivo* service conditions. When feasible, test specimens should be loaded in a manner that simulates *in vivo* conditions, both in magnitude and type of loading. Clinically relevant cyclic load tests may include testing to failure or for a specified number of cycles followed by testing to evaluate physicochemical properties.

5.3.2.1 *Static Loading*—It is notable that for some polymeric materials it has been shown that a constant load results in the same failure mechanism (for example, creep) and is the worst case when compared to a cyclic load (where the maximum amplitude of the cyclic load is equal to the constant load). Thus, in specific cases it may be acceptable to simplify the test by using a constant load even when the anticipated *in vivo* loading is cyclic. It is encumbent upon the user of this test method to demonstrate through experiment or specific reference that this simplification is applicable to the polymer under investigation and does not alter the failure mode of the test specimen. If such evidence is not available ,it is necessary to recognize that static loading and cyclic loading are measuring different material properties and are not comparable. Using one to replace the other could lead to misinterpretation of the results.

NOTE 3—Caution must be taken to ensure that fixturing does not introduce artifactual performace or degradation issues, or both. An example is the use of rigid foam block, which restricts swelling & expansion and can elevate pull out strength test results from sample compression within the block. Additionally, restricted perfusion due to the closed cell nature of the foam can result in concentration of acidic byproducts that result in accelerated degradation when compared to a normally perfused and buffered *in vivo* condition.

NOTE 4—When performing degradation testing under load, it may be necessary to consider and monitor polymer creep during testing, which may be significant.

5.4 Absorbable devices subjected to flow conditions (for example, vascular stents, particularly those with a drug eluting component) may degrade more rapidly than the same device maintained under static degradation test conditions. When it is feasible to estimate the flow conditions that an implant will be subjected to *in vivo* and replicate them *in vitro* the degradation study should be conducted under flow conditions. However,

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

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

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 molar mass 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. The experimenter is cautioned that at lower ratios (that is, less buffering capacity) the solution pH may change more quickly. To provide adequate buffer capacity, solution-to-HDP mass ratio is recommended to be greater than 30:1. 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 of the soaking solution 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 ± 1°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 mass of a sample to a precision of 0.1 % of its initial mass. 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 *Mass Loss*—A minimum of three samples shall be tested per time period.

7.2 *Molar Mass*—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 5—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 required test period is dependent on the degradation rate of the test polymer, the solution/specimen mass ratio, and the solution's buffering capacity; once per week is generally practical and suggested. In cases where no prior knowledge of the degradation rate is available, it is suggested that the pH be tested at least daily until a baseline is established. This increased sampling frequency may need to be repeated during periods of elevated mass loss (that is, pH change).

8. Sample and Test Specimen

8.1 All test samples shall be representative of the material under evaluation.

8.1.1 For most HDP resins, inter-lot variations in the molar mass and residual monomer content can be significant. Since these factors can strongly affect degradation rates, molar mass (or inherent viscosity) and residual monomer content of the source resin and fabricated test parts need to be understood.

8.1.2 Where evaluation aims allow, it is recommended that samples comparing variations in design be produced from the same material lot (or batch) and under the same fabrication conditions.

8.1.3 When testing for inter-lot variability in degradation rate (for example, for process validation purposes), a minimum of three resin lots should be used.

8.2 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. Unsterilized control specimens may be included for comparative purposes showing the effects of sterilization.

9. Procedure

9.1 *Test A, Mass Loss:*

9.1.1 Test samples, in either resin or fabricated form, shall be weighed to a precision of 0.1 % of the total sample mass prior to placement in the physiological solution. Samples shall be dried to a constant mass before initial weighing (see Note 6 and X1.8). Drying conditions, including final relative humidity (if applicable), shall be reported and may include the use of a desiccator, partial vacuum, or elevated temperatures (see Note 7).

9.1.2 Test samples shall be fully immersed in the physiological solution for a specified period of time as discussed in 4.1 (for example, 1 week, 2 weeks, and so forth).

9.1.3 Upon completion of the specified time period, each sample shall be removed, gently rinsed with sufficient distilled water to remove saline, placed in a tared container, and dried to a constant mass (see Note 6 and X1.8). The weight shall be recorded to a precision of 0.1 % of the original total sample mass.

NOTE 6—Drying to a constant mass may be quantified as less than 0.1 % mass change over a period of 48 h, or less than 0.05 % change in 24 h if the balance used is capable of such precision. Section X1.8 provides additional information.

NOTE 7—Elevated temperatures may be used to assist drying of the sample provided that the temperature used does not induce material or chemical changes in the sample. Vacuum drying with a dry gas purge can alternately be used without concern for material degradation. The drying conditions used for the samples prior to aging and for the samples retrieved at each test interval shall be identical. The actual drying conditions used are to be reported.

NOTE 8—Sample debris/fragments may be produced during the degradation study. It may not be appropriate or relevant to consider separated debris/fragments as part of the test sample mass. In such cases, collection and measurement of sample fragments are optional. In the event that recovery and quantification are needed, refer to ISO 13781, Clause "Separation of samples and debris."

9.1.4 After weighing, the samples shall not be returned to the physiological solution and shall be retired from the degradation study. Dried samples from the measurement of mass loss shall not be used for mechanical testing, but can be reused for evaluation of changes in molar mass (9.2) or other non-mechanical testing (e.g., differential scanning calorimetry, etc.).

9.2 *Test B, Molar Mass:*

9.2.1 Prior to placement of samples in the physiological solution, determine the molar mass of representative samples using either inherent viscosity (logarithmic viscosity number) testing following the recommendations of Test Method D2857 or size exclusion chromatography. Testing shall be done in a solvent appropriate for the test polymer and at a temperature sufficient to allow solubility and temperature control. For example, the molar mass of poly(*l*-lactide) should be determined in chloroform at 30°C. The sample dilution ratio (mg/cm^3) and test temperature shall be reported. Alternative means of molar mass determination may be used when feasible.

9.2.2 Test samples shall be fully immersed in the physiological solution for the specified period of time (for example, 1 week, 3 weeks, 52 weeks, and so forth).

9.2.3 Samples shall be removed at each specified time period throughout the duration of the test, dried as in 9.1.1, and tested for inherent viscosity or size exclusion chromatography for degradation monitoring as above. For polymers that undergo very rapid degradation, the molar mass may change significantly during the drying procedure, causing an overestimate of the degradation rate. Therefore the user should exercise caution in interpretation of this data. This caution does not generally apply to mass loss measurements, since continued degradation after the samples are placed in tared containers will not affect the sample mass unless the degradation products are volatile. For rapidly degrading HDP materials, alternative procedures such as vacuum drying should be considered.

9.3 *Test C, Mechanical Testing:*

9.3.1 Determine the appropriate mechanical properties of representative samples of resin or fabricated forms using tensile, compressive, torque, bending or other appropriate mechanical tests prior to placement of the samples in the physiological solution (time zero). Relevant ASTM test methods may include one or more of the following:

Test Method D638
Test Method D671
Test Method D695
Test Method D747
Test Method D790
Test Method D882
Test Method D1708
Test Method D1822

9.3.2 Fully immerse test samples in the physiological solution at 37°C for the specified period of time (for example, 1 week, 2 weeks, and so forth).

9.3.3 Remove samples at each specified time period throughout the duration of the study and test using the originally selected mechanical test methods and conditions. Unless otherwise deemed relevant, samples should be tested in a non-dried or wet condition. Section X1.9 provides additional information. Testing conditions, wet versus dry, testing temperature, and so forth, should be reported.

9.3.4 Unless specifically germane to the testing scheme, samples shall be retired after the completion of each test.

9.4 *Other Testing:*

9.4.1 The characterization of other material properties and use of other test methods (for example, thermal properties measured using Differential Scanning Calorimetry) may also be performed at each test interval. Conditioning and testing parameters, as well as test results, should all be recorded and reported.

9.4.2 The degradation products of the HDP under investigation may be analyzed. ISO 10993–9 provides guidelines for identification and quantification of degradation products.

9.4.3 Biological response to HDP materials or their degradation products may be investigated. Practice F748 and ISO 10993–1 provide guidelines for the selection of *in vitro* and *in vivo* biocompatibility tests for medical devices and materials.

10. Test Termination

10.1 Testing of samples shall be terminated when one or more of the following has occurred:

10.1.1 A predetermined end point has been reached, that is, elapsed time (for example, 2 years), percent mass loss, minimum molar mass, percent strength loss, and so forth.

10.1.2 Sample integrity has been compromised by the progression of degradation or by mechanical damage to the point that meaningful and reliable data may no longer be obtained.

10.1.3 The soaking solution temperature or pH has drifted outside of the ranges specified in Section 6. Any sample properties obtained since the last in-range temperature and pH measurements shall be considered invalid and so noted in the study report (see X1.4).

11. Report

11.1 Report the following information:

11.1.1 Test material description, batch or lot number and dimensions (as appropriate).

11.1.2 Solution composition and preparation procedures.

11.1.3 Measurements of solution temperature and pH with time, if applicable.

11.1.4 Sample mass expressed as an average percentage loss, initial and subsequent by time period.

11.1.5 Molar mass, initial and subsequent by time period.

11.1.6 Mechanical properties (tensile strength, compressive strength, stiffness, elongation at break, and so forth) appropriate for tests performed, at time zero and at each time period.

11.1.7 Other material properties measured.

11.1.8 Reason(s) for test termination.

12. Precision

12.1 Intralaboratory and interlaboratory reproducibility has not been systematically determined.

13. Keywords

13.1 absorbable; bioabsorbable; degradation; *in vitro*; hydrolytically degradable polymer; hydrolysis; PLA, poly(*l*-lactic acid); poly(*d*-lactide); poly(*d,l*-lactide); PGA, poly(glycolide); poly(caprolactone); poly(*p*-dioxanone); surgical implant

APPENDIXES

(Nonmandatory Information)

X1. RATIONALE

X1.1 With the development of absorbable polymers for use in implantable devices, there is a need to define standard testing methods that aid in characterizing material and mechanical properties with time in a simulated physiological environment. This test method is intended only as a framework for assessing degradation of implant materials and devices.

X1.1.1 This test method is written for use in characterizing hydrolytically degradable polymer resins and devices. Given the wide variety of absorbable polymer compositions currently available or under investigation, it is incumbent upon the researcher to show through reference or experimentation that other degradation mechanisms are not dominant for the material and the intended use. For example, certain bio-polymers (for example, collagen based materials such as gelatin) are known to degrade *in vivo* primarily by enzymatic attack and the use of this method would give a serious underestimation of the degradation rate. It has also been hypothesized that enzymatic degradation may play a role in the degradation of some synthetic polymers. *in vitro* studies have shown that in sufficient concentration certain enzymes (for example, esterases) may increase degradation rates of specific polymers with susceptible bonds. However, when comparisons have been made between *in vitro* and *in vivo* degradation rates of equivalent samples of hydrolytically degradable polymers under unloaded conditions, the results have consistently shown that *in vivo* acceleration of degradation is either not present or is within the error of measurement.[7]

X1.2 It is recognized that the use of test coupons or specimens in forms other than final implant configurations may be helpful in assessing relevant polymer properties. For example, rectangular or round rods may be necessary to measure flexural properties, while a screw geometry may be required to evaluate the performance of a specific implantable device. However, specimen size, surface area, and process considerations must be addressed in order to relate *in vitro* degradation of test specimens to *in vivo* behavior of implant devices.

X1.3 The pH level specified for the buffered saline solution (that is, 7.4 ± 0.2) was selected on the basis of information received from two consultants to the Task Group that this range of pH values was representative of that found in human blood and extra-cellular fluid. For devices intended for use in applications where the fluid environment has a different pH (for example, urethral stents exposed to urine), a different pH specification may be more appropriate. It is then incumbent upon the researcher to properly document the choice of environmental conditions. The range of ±0.2 should be maintained regardless of the chosen target value of pH.

X1.3.1 For this application, the time weighted average (TWA) pH is computed using the following equation:

$$\text{TWA pH} = \frac{(\text{pH}_1\, t_1)+(\text{pH}_2\, t_2)+(\text{pH}_3\, t_3)+\ldots+(\text{pH}_n\, t_n)}{(t_1+t_2+t_3+\ldots+t_n)} \quad \text{(X1.1)}$$

where:

pH = measured pH at the respective sampling point,
t_1 = elapsed time from buffer replenishment, and
t_n = elapsed time from the prior sampling point.

X1.3.2 It is also recommended that the starting pH of the solution be made as close to the upper end of the chosen range as possible since all known HDP systems generate degradation products that are acidic.

X1.3.3 Information regarding the actual impact both alkaline (pH = 10.09) and acidic (pH = 5.25) pH has on the mechanical properties of absorbable sutures (as observed at pH = 7.44) can be found in Chu.[8]

X1.4 Termination of testing, following a significant change in solution temperature or pH, is indicated in 10.1.3 in order to avoid the generation of invalid results once meaningful loss of control over soaking conditions has occurred.

X1.5 A wide variety of PBS compositions is available and in common use. The components are targeted to achieve final solutions that exert near-physiological osmotic pressures of approximately 280 to 300 mOsm. Common buffer concentrations range from approximately 0.01 to 0.1 M with the higher concentrations providing greater buffering capacity. Additional information about the composition and preparation of pH proportioned monobasic-dibasic phosphate buffer solutions may be found in a handbook available from Calbiochem Inc., a division of EMD Biosciences.[9]

X1.6 Addition of sodium azide at a concentration of 0.1 % is common. Other anitimicrobials that are commonly used include penicillin (100 U/mL), streptomycin (100 µg/mL), and amphotericin (0.25 to 2.5 µg/mL). Regardless of the antibiotic or antimicrobial agent(s) that is used, it is incumbent upon the investigator to determine that their use does not affect the degradation rate of the HDP under investigation. These materials may be hazardous and all persons using them should review the MSDS before handling and use all recommended safety precautions.

X1.7 The inert containers used to hold the samples and solution are usually glass or plastic. However, for some (short duration) tests, stainless steel containers may be appropriate.

X1.8 Revision or further specification of requirements for drying to a constant mass are intended to be developed from round robin testing to follow issuance of this test method. The requirements stated in Note 6 are based on experience with extruded 3.2-mm diameter rods of *l*-PLA dried under nominal full vacuum at room temperature. Constant mass was achieved after 3 to 4 days.

X1.9 Task Group members have observed the use of wet versus dry test conditions to result in significant differences in some mechanical property measurements. It is recommended that testing be performed on specimens that are immersed in water at 37°C at the time of testing. Report whichever conditions are actually used.

X1.10 This test method does not suggest the use of agitation during soaking for the following reasons. First, in the majority of applications for absorbable polymers, implantation occurs in tissues that will not expose the implants to measurable fluid flow. Even in cases where turnover of fluids occurs, such as in the abdominal cavity, the device will become encapsulated in fibrous tissue within two weeks of implantation. The presence of the fibrous capsule will shield the material from fluid flow and limit transport mechanisms to diffusion. Furthermore, studies comparing static *in vitro* degradation rates to *in vivo* degradation rates for several HDP materials have shown that the *in vitro* results are predictive of the *in vivo* degradation rates.[7]

[8] Chu, C. C., "The Effect of pH on the *in vitro* Degradation of Poly(glycolide lactide) Copolymer Absorbable Sutures," *Journal of Biomedical Materials Research*, 16, 1982, pp. 117-124.

[9] Available from EMD Biosciences, Inc., 10394 Pacific Center Ct., San Diego, CA 92121. http://www.emdbiosciences.com

X2. TERMINOLOGY

X2.1 Synthetic implants fabricated from hydrolysable alpha-hydroxy polyesters have been described as "absorbable" since the first polyglycolide based sutures were commercialized in the United States in the 1970s. At that time, both poly(glycolide) (DEXON - Davis & Geck) and poly(glycolide-co-lactide) copolymer (VICRYL - Ethicon) based sutures were classified as "Absorbable Surgical Suture" by the United States Pharmacopeia (USP) and the United States Food & Drug Administration (US-FDA), a designation that remains to this day. In contrast with "Nonabsorbable Surgical Suture," synthetic glycolide-lactide and collagen based sutures undergo hydrolytic and/or enzymatic driven chain scission, generating byproducts that are then absorbed by the body. Since designation, other terms such as "degradable" and "resorbable" have been used interchangeably to describe absorbable implants, with the prefix "bio-" often applied to all these terms.

X2.2 Based on historical usage and regulatory precedent, this document preferentially utilizes the term absorb/absorbable/absorption to describe implantable synthetic hydrolysable polymers & devices. The prefix "bio" is avoided since it is redundant in the context of implant applications. "Resorb" and its derivatives are avoided since they are accepted medical terms routinely utilized to describe natural resorption processes present in dynamic tissue, such as osteoclastic driven bone remodeling. "Degrade" and its various derivatives are avoided when referring categorically to either an implantable device or raw material since common utilization is routinely applied

broadly to include composting and other natural processes (including ultra-violet radiation) that cause materials to either intentionally or unintentionally break down into chemical and/or particulate matter. However, use of the term "degrade" and its derivatives is considered acceptable when specifically referring to chain scission within the implantable device or polymer (e.g. "The absorbable implant degrades through hydrolysis." or "During extrusion, absorbable polyglycolide is prone to thermal degradation.").

X2.3 Since a variety of alternative terms to absorbable have been historically utilized interchangeably both within and across surgical disciplines (but intermittently with inferred differentiation), the user of this document is cautioned that effective searches of the published literature should include all potential terms used to describe an absorbable implant or material. These include, but are not limited to the following:

X2.3.1 Absorbable and its derivatives.

X2.3.2 Bioabsorbable and its derivatives.

X2.3.3 Degradable and its derivatives.

X2.3.4 Biodegradable and its derivatives.

X2.3.5 Resorbable and its derivatives.

X2.3.6 Bioresorbable and its derivatives.