INTERNATIONAL STANDARD

ISO 13781

Second edition
2017-07

Implants for surgery — Homopolymers, copolymers and blends on poly(lactide) — In vitro degradation testing

Implants chirurgicaux — Homopolymères, copolymères et mélanges sur poly(lactide) — Essais de dégradation in vitro

Reference number
ISO 13781:2017(E)

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Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see the following URL: www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 150, *Implants for surgery,* Subcommittee SC 1, *Materials.*

This second edition cancels and replaces the first edition (ISO 13781:1997) and ISO 15814, which have been technically revised.

The main change compared to the previous edition is as follows:

— the principle contents of ISO 15814 are incorporated into this document.

Introduction

With the development of absorbable polymers for use in implantable devices, there is a need to define standard test methods to evaluate the behaviour of bulk material or devices under simulated physiological environments. On the other hand, the behaviour of absorbable materials and devices *in situ* depends on the conditions in which the material is implanted. These conditions differ, so that the site-specific behaviour of the material or device can differ. The interpretation of *in vitro* test results therefore needs to be considered carefully, taking into account any correlation of test results under *in vitro* and *in vivo* conditions. Only functional *in vivo* tests with the final product can answer actual degradation behaviour *in situ*.

Implants for surgery — Homopolymers, copolymers and blends on poly(lactide) — In vitro degradation testing

1 Scope

This document describes methods for the determination of chemical and mechanical changes in poly(lactide)-based homopolymers, copolymers and/or blends induced under *in vitro* degradation testing conditions. This document covers polymers based on L-lactide, D-lactide, and/or D, L-lactide monomeric units.

The purpose of this document is to compare and/or evaluate materials or processing conditions. This document also describes the fundamental physical and mechanical evaluations needed for an *in vitro* degradation characterization of an absorbable poly(lactide) or other hydrolysable material or device.

This document is applicable to poly(lactide)-based homopolymers, copolymers and/or blends in bulk or processed forms and used for the manufacture of surgical implants, including finished products (packaged and sterilized implants).

The test methods specified in this document are also intended to determine the *in vitro* degradation rate and related changes in material properties of polylactide-based copolymers and/or blends with various other comonomers, such as glycolid, trimethylene, carbonate and/or ε-caprolactone. Unless otherwise validated for a specific device, these *in vitro* methods cannot be used to definitively predict device behaviour under *in vivo* conditions.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 178, *Plastics — Determination of flexural properties*

ISO 180, *Plastics — Determination of Izod impact strength*

ISO 527-1, *Plastics — Determination of tensile properties — Part 1: General principles*

ISO 527-2, *Plastics — Determination of tensile properties — Part 2: Test conditions for moulding and extrusion plastics*

ISO 527-3, *Plastics — Determination of tensile properties — Part 3: Test conditions for films and sheets*

ISO 604,*Plastics — Determination of compressive properties*

ISO 1628-1, *Plastics — Determination of the viscosity of polymers in dilute solution using capillary viscometers — Part 1: General principles*

ISO 1805, *Fishing nets — Determination of breaking force and knot breaking force of netting yarns*

ISO 2062, *Textiles — Yarns from packages — Determination of single-end breaking force and elongation at break using constant rate of extension (CRE) tester*

ISO 6721-2, *Plastics — Determination of dynamic mechanical properties — Part 2: Torsion-pendulum method*

ISO 13934-1, *Textiles — Tensile properties of fabrics — Part 1: Determination of maximum force and elongation at maximum force using the strip method*

ISO 14130, *Fibre-reinforced plastic composites — Determination of apparent interlaminar shear strength by short-beam method*

ISO 16014-1, *Plastics — Determination of average molecular mass and molecular mass distribution of polymers using size-exclusion chromatography — Part 1: General principles*

ISO 16014-2, *Plastics — Determination of average molecular mass and molecular mass distribution of polymers using size-exclusion chromatography — Part 2: Universal calibration method*

ISO 16014-3, *Plastics — Determination of average molecular mass and molecular mass distribution of polymers using size-exclusion chromatography — Part 3: Low-temperature method*

ISO 16014-4, *Plastics — Determination of average molecular mass and molecular mass distribution of polymers using size-exclusion chromatography — Part 4: High-temperature method*

ISO 16014-5, *Plastics — Determination of average molecular mass and molecular mass distribution of polymers using size-exclusion chromatography — Part 5: Method using light-scattering detection*

ASTM D2990,*Standard test methods for tensile, compressive, and flexural creep and creep-rupture of plastics*

ASTM D5296, *Test method for molecular weight averages and molecular weight distribution of polystyrene by high performance size-exclusion chromatography*

ASTM F1635-16, *Standard test method for in vitro degradation testing of hydrolytically degradable polymer resins and fabricated forms for surgical implants*

ASTM F2902-16, *Standard guide for assessment of absorbable polymeric implants*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— IEC Electropedia: available at http://www.electropedia.org/

— ISO Online browsing platform: available at http://www.iso.org/obp

NOTE A discussion regarding the basis for some of the terms and definitions in this clause is available in Annex A.

3.1
absorbable polymer
non-endogenous (foreign) polymeric material that is capable of passing through or being assimilated by cells and/or tissue over time

3.2
absorption
act of a non-endogenous (foreign) material or substance passing through or being assimilated by cells and/or tissue over time

3.3
blend
physical mixture of two or more different thermoplastic polymers and/or *copolymers* (3.4)

3.4
copolymer
polymer synthesized by polymerizing two or more monomer units together

3.5
***in vitro* degradation**
loss of mechanical properties and/or chemical integrity through chemical changes induced by a simulated physiological environment

3.6
poly(D,L-lactide)
polymer synthesized with approximately equimolar concentrations of D-lactide and L-lactide monomeric units

3.7
poly(L-lactide)
polymer synthesized exclusively from L-lactide monomeric units

3.8
sample
finite subset, object or individual of a group, class or population whose properties or characteristics are studied to gain information regarding the whole

3.9
specimen
specific portion or quantity of a sample utilized to obtain a single measurement of a property or characteristic

4 Degradation evaluation

4.1 General

Appropriate *in vitro* characterization of the degradation of an absorbable polymeric material monitors the progressive loss of both sample mass and molar mass (i.e. molecular weight) from ongoing exposure to a physiologically relevant environment. Such an environment provides fluid and thermal conditions that generate an *in vitro* degradation rate that approximates the rate observed *in vivo*. Such an *in vitro* degradation characterization also monitors the loss of device-relevant mechanical properties over time. Thus, unless justified otherwise, such a material or device degradation characterization shall include a systematic monitoring of the loss of sample mass (see 5.2), molar mass (via inherent viscosity and/or GPC/SEC, see 5.3) and at least one mechanical property that can be considered relevant to the characteristics and intended use of the device (see 5.4).

The degradation rate of an absorbable material or device can be affected by sample dimensions and other manufacturing/processing parameters (e.g. fibre draw ratio). As the shape and the structure of the test sample can have a strong influence on the degradation kinetics, where applicable, the initial test sample should be comparable to the intended product in shape and structure (i.e. fibre, film, plate, rod, bulk material or other relevant form, as appropriate). The test sample may be a finished product or a test coupon fabricated to emulate the relevant physical and/or mechanical properties of the intended product.

Evaluation of samples representative of the finished product shall be conducted following terminal sterilization at a level that meets or exceeds anticipated commercial exposure.

While the described general degradation evaluations and related tests can be useful toward characterizing a finished product, they are not necessarily adequate to address all device-specific issues. For example, a device that undergoes *in vivo* loading can degrade significantly faster than an identical device implanted in an unloaded application. Thus, a device that is intended to undergo *in vivo* loading should be additionally evaluated *in vitro* under real-time degradation conditions that approximate the anticipated mechanical loading, including, if applicable, cyclic loading, shear, creep loading, with further guidance available in ASTM F2902-16, 6.2.2.2.

The initial values for all tests shall be determined directly before starting the degradation test (time zero). All subsequent tests shall be carried out on degraded samples at each test interval. The presence or absence of a need for load testing should be based on a developed understanding of the device and any related safety concerns at the time of loading. Such an assessment should incorporate any needed considerations for extreme limits and/or creep aspects of the loading.

When load testing, attention should be directed toward mitigating any potential effects that fixturing may have on the degradation rate of the device. For example, constriction of a fixtured device with a moisture barrier on one or more sides carries potential to inhibit outward diffusion of acidic degradation products that could thereby affect the device's interstitial pH and accelerate degradation. Physical constriction also carries potential to inhibit normal device swelling, which, as a result, carries potential to induce artifacts in the mechanical response being measured.

4.2 Apparatus and reagents

4.2.1 Soaking solution

4.2.1.1 General

For the *in vitro* degradation study, the test sample shall be immersed in a Sörensen or other suitable pH 7,4 buffer solution. However, if the normal pH of the intended *in vivo* application is not pH 7,4 (e.g. synovial fluid, portions of the alimentary canal), other appropriate pH and buffer solutions may be used. For pH 7,4 applications, suitable solutions typically contain potassium dihydrogenphosphate and disodium hydrogenphosphate in analytical water (e.g. Grade 2 in accordance with ISO 3696) and include phosphate buffered saline (140 mM NaCl, 10 mM phosphate buffer and 3 mM KCl), commonly known as "PBS". The salts used for the preparation of the buffer solution shall be of analytical grade and dried to constant mass. Any utilized buffer solution should have sufficient buffer capacity to allow maintenance of the appropriate targeted pH to within ±0,2 pH units throughout the degradation process. The adequacy of buffer systems that encounter excursions outside these limits can assessed by determining the time weighted average, more details of which may be found in ASTM F1635-16, 6.1 and X1.3.1.

4.2.1.2 Preparation of Sörensen buffer solution

If a Sörensen solution is used, it shall be prepared by mixing 18,2 % (volume fraction) from solution A and 81,8 % (volume fraction) from solution B.

— Solution A: 1/15 mol/L KH_2PO_4, prepared by dissolving 9,08 g KH_2PO_4 in 1 l water.

— Solution B: 1/15 mol/L Na_2HPO_4, prepared by dissolving 11,9 g $Na_2HPO_4 \bullet 2H_2O$ in 1 l water.

When prepared in this manner, the pH value of this buffer solution will be 7,4 ± 0,2.

4.2.2 Sample container

The container (e.g. bottle, jar, vial) shall be either inert plastic or glass and capable of holding the test sample for each material and time interval and the required volume of soaking solution. Each container shall be sealable against loss of solution by evaporation and to prevent microbial contamination.

4.2.3 Constant-temperature bath or oven

The constant-temperature bath or oven (for example, circulating air dryer) shall be capable of maintaining all the sample containers at the specified degradation temperature ±1 °C for the specified test duration.

4.2.4 pH-meter

A pH-meter with a precision of 0,02 or better shall be used to monitor for pH change. A pH-meter with a calibrated accuracy of 0,02 or better shall be used to determine pH.

4.2.5 Balance

A calibrated balance shall be used to monitor mass loss in the samples. The precision of the balance shall be sufficient to measure mass changes equal to or less than 0,1 % of the original dry mass of the samples.

4.3 Real-time degradation — Sample conditioning procedure

4.3.1 Sample loading and placement

Before beginning real-time degradation, determine initial mass in accordance with 5.2.3.1.

Place the test sample into a container (4.2.3) with soaking solution (4.2.1) and seal the container. The test sample shall be fully immersed in the soaking solution.

The minimum volume of the buffer solution used shall be 10 ml. To provide adequate buffer capacity, the ratio of volume of the buffer solution, in millilitres, to the test sample mass, in grams, is recommended to be greater than 30:1. However, the actual buffer capacity shall be equal or greater than the maximum calculated post-hydrolysis acid concentration.

4.3.2 Control of temperature

Using the constant-temperature bath or oven (4.2.4), maintain the test sample containers at physiological temperature of (37 ± 1) °C.

4.3.3 Control of buffer solution

4.3.3.1 Changes in pH value

The pH of the buffer solution shall be measured in at least two different containers at each test interval or every six weeks, whichever is shorter. However, unless prior experience indicates otherwise, monitoring should preferably be undertaken weekly (or more frequently, if needed).

If in one container the pH value has shifted beyond the limits, measure the value in all containers and adjust, as needed, to the appropriate targeted pH ± 0,2. If encountered, assess the acceptability of any excursion beyond pH ± 0,2 in accordance with the provisions of ASTM F1635-16, 6.1 and X1.3.1.

For samples designated solely for mechanical evaluation per 5.4, the buffer solution can be replaced instead of adjusted, providing such fluid replacement does not compromise the mechanical integrity of the degraded sample.

4.3.3.2 Clouding of buffer solution

Clouding of the buffer solution may indicate the contamination with microorganisms. Discard the test sample if any clouding is visible which cannot be related directly to the material itself or its degradation products.

It is recommended that the containers and soaking solutions be sterilized in order to avoid contamination with microorganisms.

4.3.4 Sample retrieval

Remove the samples from the soaking solution and test according to the selected Clause 5 tests at predetermined intervals.

Test sample retrieval intervals shall be selected to both maintain clinical relevance and profile the degradation properties of the device. Mechanical properties shall be profiled from an initial clinically relevant condition until a point where measurement of the mechanical attribute becomes impractical. Additionally, mechanical properties of the device at the point of full hydration should also be understood. Thus, dependent on the intended clinical application, potential retrieval durations could range from less than a minute (i.e. minimal soaking solution exposure) to extended time intervals for the generation of samples with marginal mechanical strength. In addition, when determining the physical or molar mass of degraded samples, retrieval durations may be extended beyond the threshold of mechanical integrity to allow evaluation of fragmented particles. As a result and dependent on the specific attribute being measured, retrieval intervals may vary for the same device. Thus, to adequately characterize each measured attribute, a minimum of an initial sample and retrieved samples from at least five relatively evenly spaced degradation intervals shall be evaluated, with additional data points potentially necessary for adequate characterization of complex profiles.

NOTE As degradation proceeds, physically independent manipulation and mechanical measurement of the sample will eventually become impossible. Thus, before evaluating a large quantity of samples, it is suggested to conduct a pilot evaluation to better ascertain appropriate sample retrieval timing and quantities.

Both fluid flow and mechanical loading carry potential to significantly influence the rate of sample degradation. If the intended use of the device is subject to either fluid flow or loading conditions, the user of this document should consult the guidance available in ASTM F1635-16 and ASTM F2902-16. If such conditions are likely to significantly affect test results, it is suggested that the degradation evaluation be undertaken in a manner that approximates the device's *in vivo* service condition. However, the nature and extent of such service conditions will be both device and application specific and are therefore beyond the scope of this document.

5 Physical, chemical and mechanical tests

5.1 General

The testing described in each of the following subclauses is considered essential for an appropriate characterization of an absorbable implant. Both the evaluation of mass loss in accordance with 5.2 and the evaluation of molar mass in accordance with 5.3 are required. Additionally required is a mechanical evaluation in accordance with 5.4 utilizing at least one test method, with additional methods potentially necessary dependent on the mechanical performance requirements of the material and/or device.

A listing of potentially useful evaluations of a device's mechanical, degradation and performance properties can be found in ASTM F2902-16, Table 2.

5.2 Loss of sample mass

5.2.1 Apparatus

5.2.1.1 Balance, a calibrated weighing device capable of measuring sample mass to the requisite precision.

5.2.1.2 Desiccator, a sealable container that retains a desiccant to absorb moisture for the purpose of drying the test samples. For example, silica gel beads containing an indicator can be used.

5.2.1.3 Vacuum pump, a pump capable of producing a vacuum with a pressure of at most 5 kPa (50 mbar) in the desiccator.

5.2.1.4 Filter system, an appropriate apparatus for the separation of the debris produced during the degradation study. This may involve an inert filter and rinse system, a temperature-controlled centrifuge, or a combination thereof. The apparatus shall be described and defined in the test report.

5.2.2 Number of test samples

At least three test samples shall be evaluated at each retrieval interval. Since mass loss is sample specific, a separate container shall be used for each mass loss sample.

5.2.3 Procedure

5.2.3.1 Measurement of initial mass

Dry each un-degraded test sample under vacuum at room temperature to constant mass. Determine the initial mass of each sample within a relative standard uncertainty of 0,1 % of its total mass.

5.2.3.2 Separation debris

Dependent on the intended application and the objective of the test, it may not be appropriate or relevant to consider separated fragments or debris as part of the test sample mass. In such cases, a mild rinsing and drying of the degrading test sample is all that is required, with recovery and quantification of fragments/debris being optional. In the event that recovery and quantification are needed, accumulate specimen fragments/debris either by a) or b).

a) By means of a filter.

   Dry a filter (<0,10 µm; if mineral included, consider pore size of <1,0 µm) under vacuum at room temperature to constant mass and determine the mass of the filter. Place the weighed filter into the filter system and lightly rinse any loose debris or fragments and residual buffer from the degraded test specimen into the filter. Subsequently, rinse the specimen and container three times with deionized water transferring all rinse liquids into the filter system to retain all possible debris. For rinsing and filtering, a water jet blast can be used.

b) By means of a centrifuge.

   Determine the mass of a clean dry centrifuge tube. Transfer the degradation test specimen solution into the centrifuge tube and close the tube prior to separation. Spin the tube in the centrifuge to obtain a firm debris pellet. Carefully decant the supernatant buffer solution into a separate container. Re-suspend the pellet with analytical water and repeat for a total of three centrifugation/decantation cycles.

5.2.3.3 Determination of degraded mass

A thorough but mild rinsing of the degraded test sample is needed to remove any loose particles or residual buffer solution that may be present on the sample, regardless of whether it was undertaken independently or as part of a fragments/debris recovery process. Once rinsing is complete, for each sample determine the following, as appropriate:

— *degraded mass*: dry the previously rinsed degraded specimen to a constant mass within a relative standard uncertainty of 0,1 % of its initial mass;

— *mass loss*: subtract the *degraded mass* from initial mass;

— *debris component mass* (optional): dry the either filtered or centrifuged debris to a constant mass within a relative standard uncertainty of 0,1 % of the specimen's initial mass;

— *soluble component mass* (optional): subtract the *debris component mass* from the *mass loss*.

5.2.4 Reusability of test specimens

Dried specimens from the measurement of mass loss shall not be used for mechanical testing (5.4). However, dried specimens may be used for further non-mechanical testing, such as loss in molar mass (5.3).

5.3 Evaluation of molar mass

5.3.1 Via inherent viscosity

The inherent viscosity of the undegraded and degraded materials dried to a constant mass shall be determined in accordance with ISO 1628-1 at a preferable test temperature of 30,0 °C ± 0,01 °C or alternatively 25,0 °C ± 0,01 °C. The solvent shall be chloroform. If the copolymer or blend is not soluble in chloroform, use hexafluroisopropanol (HFIP). The concentration of the polymer solution shall be 0,1 % with a mass concentration of (50 ± 2) mg/50 ml solution.

5.3.2 Via gel permeation chromatography/size exclusion chromatography

Gel permeation chromatography (GPC) or size exclusion chromatography (SEC) can alternatively be utilized to evaluate the molar mass of the initial and degrading absorbable material, provided that all of the following parameters are both monitored and reported for all data points:

— number-average molar mass (M_n);

— mass-average molar mass (M_w);

— z-average molar mass (M_z);

— viscosity average molar mass (M_v);

— polydispersity index.

Such an evaluation shall be conducted using methods substantially compliant with those described in ISO 16014 (all parts) or ASTM D5296. The specific type of carrier solvent and reference standards shall be the same throughout the evaluation and a description of both shall be included in the test results.

5.4 Mechanical tests

5.4.1 General

Mechanical tests shall be performed on test specimens not altered by previous testing.

NOTE Test specimens used for the determination of mechanical properties can be used for further non-mechanical testing (e.g. loss of molar mass, changes in T_g, structural analysis via scanning electron microscopy). However, when mechanical properties are measured, energy is put into the specimens and directional loads are applied. Both can alter the physicochemical properties of the material and therefore can influence the results of the investigations carried out after mechanical testing.

Each test specimen shall be used for one mechanical test only. During all test intervals, do not agitate the solution unless specified in the conditioning protocol. The test specimens shall be kept wet after removal from the soaking solution and during testing. However, careful drying of gripping surfaces (e.g. using a paper towel) is allowed to prevent slippage of the test specimen in the grips.

Specimens taken from at least three test samples shall be tested at each retrieval interval, with at least six samples at each test interval typically needed for statistical analysis.

Since mechanical testing cannot be conducted on dried specimens, multiple test specimens for each mechanical test retrieval interval may be placed in a single container, provided the pH of the solution is appropriately maintained.

5.4.2 Conditioning of test samples

Sample conditioning shall be conducted in accordance with 4.3, with sample retrieval to occur at time intervals reflective of both clinical relevance and the mechanical degradation characteristics of the device.

Specimen mechanical properties can change with both temperature and the level of hydration. The glass transition of amorphous or semicrystalline polymers depends on the water content of the material. Drying of test specimens, especially of fibre-reinforced and/or degraded materials, can affect their properties. Thus, effort should be made to ensure each (non-dry) test specimen is mechanically evaluated in a hydrated condition.

In addition to the duration of real time degradation, sample conditions at the time of testing shall also be described in the test report.

5.4.3 Test methods

The mechanical test method and parameters shall be relevant for the device and its intended use. The selected test and related parameters shall be from those standards listed in Table 1, from ASTM F2902-16, Table 2, or from other standards or other validated methods that are specific for the type of device. Additional testing specified by the parties submitting the sample or other parameters as determined by the test house can be performed. Modified or new test methods should be relevant and validated with established methods. Besides providing an understanding of normal service conditions, the selected mechanical characterization should also provide an assessment of the worst case clinical failure mode.

Although at least one mechanical test method is required as the minimum for this standard assessment, evaluation of other mechanical properties may be necessary to ensure all clinically relevant properties are assessed.

Table 1 — Mechanical test methods for consideration

Form	Test method reference
Rigid material	ISO 178 ISO 180 ISO 527-1, ISO 527-2 ISO 6721-2 ISO 604 ISO 14130 ASTM D2990
Film, foil, sheet	ISO 527-3
Fibre, textile	ISO 2062 ISO 1805 ISO 13934-1

5.5 Additional evaluation methods for consideration

Additional evaluation options are available for monitoring and/or characterizing material property changes that occur during the hydrolytic degradation process. While a non-exhaustive listing of potential additional tests is presented in Annex B, the listed methods should not necessarily be considered as appropriate, meaningful or necessary dependent on the scope of other tests being conducted and the nature of the specific device and/or intended application.

6 Test termination

Testing of degraded samples shall be terminated (be it at a retrieval interval or upon completion of the overall evaluation) when at least one of the following has occurred.

a) a predetermined time has been reached (see 4.3.4), or

b) degradation is so advanced that testing becomes meaningless or technically impossible.

Record visual observations of what is physically present at the end of the test or retrieval interval and the reason for termination, both of which shall be included in the test report.

7 Test report

The test report shall include the following information:

a) test material description, batch or lot number and dimensions (including thickness);

b) real-time degradation environment:

   1) temperature,

   2) sample retrieval intervals,

   3) fluid flow and/or loading conditions (if relevant to intended clinical application) — provide justification for selected parameters (including absence of flow or load conditioning);

c) description of test methods used (including specificity, sensitivity and quantification limits);

d) deviations from test protocol — list and provide justification for any test method deviations or modifications;

e) reason for test termination;

f) test results:

   1) appearance — describe visual appearance of test samples after different retrieval intervals,

   2) loss of sample mass:

      i) provide average percentage mass loss — (initial and subsequent) by time interval,

      ii) indicate whether the reported mass loss does or does not include fragments or debris,

      iii) report any relevant optional retrieval interval observations, such as average percentage mass retention, average debris component mass or average soluble component mass,

   3) evaluation of molar mass — provide inherent viscosity and/or GPC/SEC results as described in 5.3 (initial and subsequent) by retrieval interval,

   4) for inherent viscosity testing, report both the dissolution solvent and test temperature (in °C) and provide all test results in dl/g units,

   5) for GPC/SEC testing, report the parameters described in 5.3.2; also, report the utilized sample dissolution solvent, GPC carrier solvent, type of reference standards, and column temperature (in °C);

   6) mechanical test:

      i) provide results (initial and subsequent by retrieval interval) for at least one device relevant mechanical property:

         I) protocol description include test reference (i.e. standard) and test parameters (such as deformation speed, distance between clamps, etc.),

         II) list and provide justification for any test method deviations or modifications,

      ii) provide additional mechanical test results (initial and subsequent by retrieval interval) as needed to further characterize other relevant mechanical properties of the device:

         I) protocol description include test reference (i.e. standard) and test parameters (such as deformation speed, distance between clamps, etc.),

II) list and provide justification for any test method deviations or modifications,

iii) if mechanical testing was not conducted on a relevant mechanical property, provide a detailed justification;

g) authentication:

1) identification of the person or institution performing the test;

2) identification and dated signature of the person responsible for the report.