Designation: F 2579 – 06ε1

Standard Specification for Amorphous Poly(lactide) and Poly(lactide-co-glycolide) Resins for Surgical Implants[1]

This standard is issued under the fixed designation F 2579; 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.

ε[1] NOTE—Section 5.9 was added and figures were corrected editorially in January 2007.

1. Scope

1.1 This specification covers virgin poly(lactide) and poly(lactide-co-glycolide) resins able to be fully solvated at 30°C by either methylene chloride (dichloromethane) or chloroform (trichloromethane). The poly(*d,l*-lactide) homopolymers covered by this specification are considered to be amorphous (that is, void of crystallinity) and are polymerized either from *meso*-lactide or from equimolar (racemic) combinations of *d*-lactide and *l*-lactide. The poly(*d,l*-lactide-co-glycolide) copolymers covered by this specification are also considered to be amorphous and are co-polymerized from a combination of glycolide and either *meso*-lactide or racemic quantities of *d*-lactide and *l*-lactide, and typically possess nominal mole fractions that equal or exceed 50 % lactide.

1.2 Since poly(glycolide) is commonly abbreviated as PGA for poly(glycolic acid) and poly(lactide) is commonly abbreviated as PLA for poly(lactic acid), these polymers are commonly referred to as PGA, PLA, and PLA:PGA resins for the hydrolytic byproducts to which they respectively degrade. PLA is a term that carries no enantiomeric specificity and therefore also encompasses the isotactic *d*-PLA and *l*-PLA moieties, each of which carries potential for crystallization. Therefore, specific reference to *d,l*-PLA is essential to appropriately differentiate the amorphous atactic/syndiotactic *d,l*-lactide based polymers and copolymers covered by this specification.

1.3 This specification is not applicable to lactide based polymers or copolymers that possess isotactic polymeric segments sufficient in size to deliver potential for lactide based crystallization. This specification is not applicable to lactide-co-glycolide copolymers that possess glycolide segments sufficient in size to deliver potential for glycolide based crystallization, thereby requiring fluorinated solvents for complete dissolution under room temperature conditions. This specification is specifically not applicable to lactide-co-glycolide copolymers with glycolide mole fractions greater than or equal to 70 % (65.3 % in mass fraction). This specification is not applicable to block copolymers or to polymers or copolymers synthesized from combinations of *d*-lactide and *l*-lactide that differ by more than 1.5 total mole percent (1.5 % of total moles).

1.4 This specification addresses material characteristics of both poly(lactide) and poly(lactide-co-glycolide) resins intended for use in surgical implants and does not apply to packaged and sterilized finished implants fabricated from these materials.

1.5 As with any material, some characteristics may be altered by processing techniques (such as molding, extrusion, machining, assembly, sterilization, etc.) required for the production of a specific part or device. Therefore, properties of fabricated forms of this resin should be evaluated independently using appropriate test methods to assure safety and efficacy.

1.6 *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 1505 Test Method for Density of Plastics by the Density-Gradient Technique

D 1898 Practice for Sampling of Plastics[3]

D 2857 Practice for Dilute Solution Viscosity of Polymers

D 3536 Test Method for Molecular Weight Averages and Molecular Weight Distribution of Polystyrene by Liquir Exclusion Chromatography (Gel Permeation Chromatography-GPC)[3]

D 3593 Test Method for Molecular Weight Averages and Molecular Weight Distribution of Certain Polymers by Liquid Size-Exclusion Chromatography (Gel Permeation Chromatography GPC) Using Universal Calibration[3]

[1] This specification is under the jurisdiction of ASTM Committee F04 on Medical and Surgical Materials and Devices and is the direct responsibility of Subcommittee F04.11 on Polymeric Materials.

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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] Withdrawn.

D 4603 Test Method for Determining Inherent Viscosity of Poly(Ethylene Terephthalate) (PET) by Glass Capillary Viscometer

E 386 Practice for Data Presentation Relating to High-Resolution Nuclear Magnetic Resonance (NMR) Spectroscopy

E 1252 Practice for General Techniques for Obtaining Infrared Spectra for Qualitative Analysis

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

2.2 *Other Documents:*

United States Pharmacopeia (USP), Edition 26[4]

ISO 10993-9, Biological Evaluation of Medical Devices, Part 9: Degradation of Materials Related to Biological Testing, Annex A[5]

ICH Q3C(R3) International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, Quality Guideline: Impurities: Residual Solvents[6]

21 CFR 820 Code of Federal Regulations, Title 21, Part 820, Quality System Regulation[7]

ANSI/ISO/ASQ Q9000 Quality Management Systems, Fundamentals and Vocabulary[8]

ANSI/ISO/ASQ Q9001 Requirements[8]

3. Terminology

3.1 *Definition:*

3.1.1 *virgin polymer*—the initially delivered form of a polymer as synthesized from its monomers and prior to any processing or fabrication into a medical device.

4. Materials and Manufacture

4.1 All raw monomer components and other materials contacting either the raw monomer(s) or resin product shall be of a quality suitable to allow for use of such resin in the manufacture of an implantable medical product. Such quality includes adequate control of particles and other potential contaminants that may affect either the toxicity of or the cell response to the as-implanted or degrading final product.

4.2 All polymer manufacturing (including monomer handling, synthesis, pelletization/grinding and all subsequent) shall be undertaken under conditions suitable to allow for use of such resin in the manufacture of an implantable medical product.

5. Chemical Composition

5.1 The amorphous poly(*d,l*-lactide) polymers covered by this specification shall be composed either of *meso*-lactide or a racemic combination of *d*-lactide and *l*-lactide. The amorphous poly(*d,l*-lactide-co-glycolide) copolymers covered by this specification can be of variable copolymer ratios and shall be composed of a combination of glycolide and either *meso*-lactide or a racemic combination of *d*-lactide and *l*-lactide where the glycolide mole fraction is less than 70 % (65.3 % in mass fraction). To assure such composition and the attainment of the desired properties, the following tests are to be conducted.

5.2 *Chemical Identification*:

5.2.1 The identity of the virgin polymer shall be confirmed either by infrared, ^{1}H-NMR, or ^{13}C-NMR spectroscopy.

5.2.2 *Infrared Identification*:

5.2.2.1 Identity of either poly(lactide) homopolymer or poly(lactide-co-glycolide) copolymer may be confirmed through an infrared spectrum exhibiting major absorption bands only at the wavelengths that appear in a suitable reference spectrum. Analysis shall be conducted using infrared spectroscopy practices similar to those described in Practice E 1252. A typical infrared transmission reference spectrum and a typical infrared absorption reference spectrum for *d,l*-PLA homopolymer are shown in Fig. 1. While poly(lactide-co-glycolide) copolymers will each have their own respective spectrum that will vary in response to copolymer ratio, this analytic method typically lacks sensitivity sufficient for quantification of copolymer ratio as specified in 7.1.2.

5.2.2.2 Additional spectral bands may be indicative of sample crystallinity or either known or unknown impurities, including residual monomer, solvents, and catalysts (refer to limits specified in Table 1).

5.2.3 *Proton Nuclear Magnetic Resonance (^{1}H-NMR) Identification*:

5.2.3.1 Identity of either poly(lactide) homopolymer or poly(lactide-co-glycolide) copolymer may be confirmed through sample dissolution, ^{1}H-NMR spectroscopy, and the use of a suitable reference spectrum. Sample dissolution is in either deuterated chloroform, deuterated dichoromethane (methylenechloride) or other substantially proton-free solvent able to fully solvate the specimen without inducing competing spectral bands. Analysis shall be conducted using practices similar to those described in Practice E 386.

5.2.3.2 Additional spectral bands may be indicative of known or unknown impurities, including residual monomer, solvents, and catalysts (refer to limits specified in Table 1).

5.2.4 *Carbon-13 Nuclear Magnetic Resonance (^{13}C-NMR) Identification*:

5.2.4.1 Identity of either poly(lactide) homopolymer or poly(lactide-co-glycolide) copolymer may be confirmed in a solid state through ^{13}C-NMR spectroscopy and the use of a suitable reference spectrum. Analysis shall be conducted using practices similar to those described in Practice E 386.

5.2.4.2 Additional spectral bands may be indicative of known or unknown impurities, including residual solvents and catalysts (refer to limits specified in Table 1).

5.3 *Specific Rotation*:

5.3.1 The virgin polymer shall have a specific rotation of –2.5 to +2.5 degrees when measured in either chloroform,

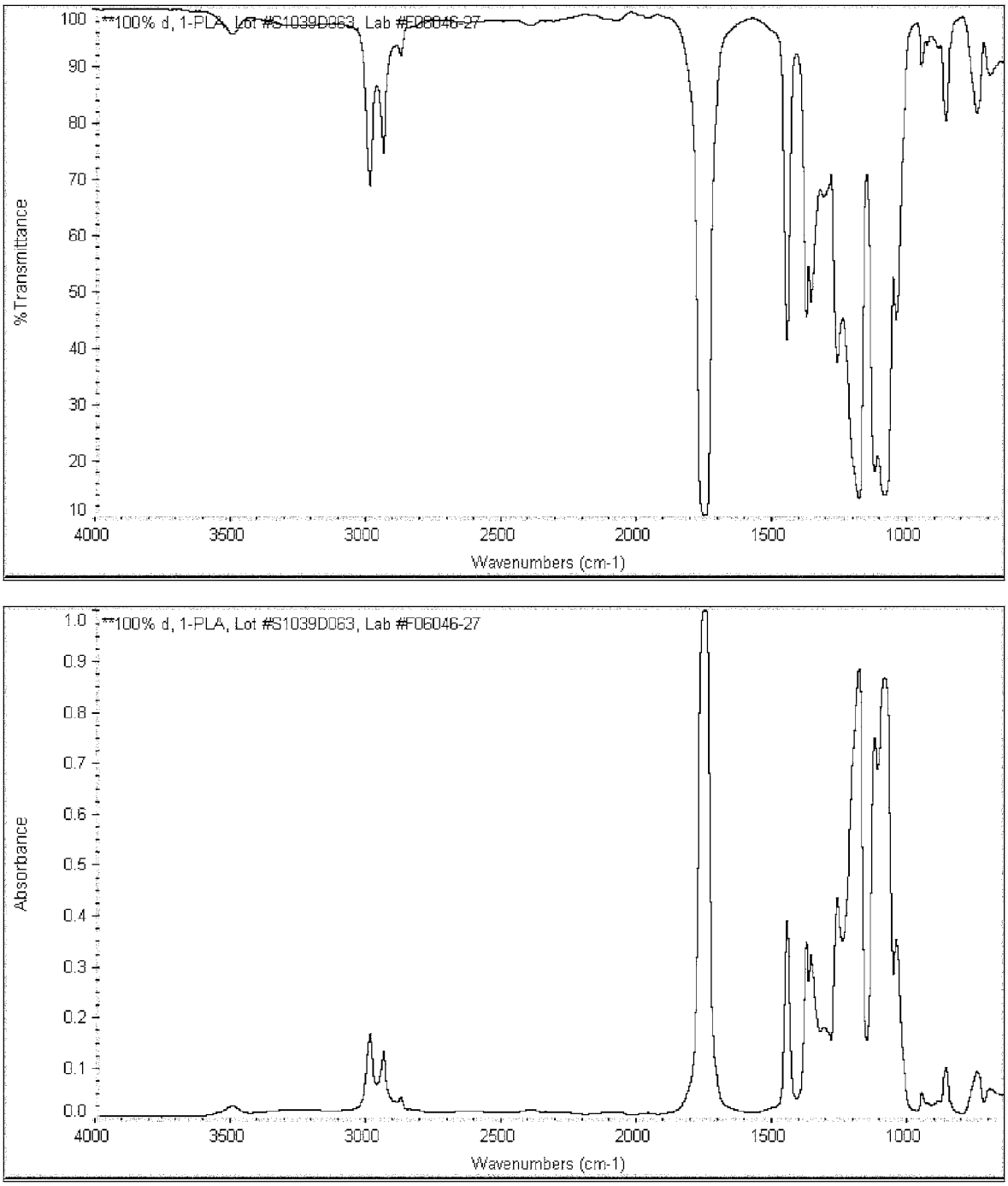
[4] Available from U.S. Pharmacopeia (USP), 12601 Twinbrook Pkwy., Rockville, MD 20852-1790, http://www.usp.org.

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

[6] Available from ICH Secretariat, c/o IFPMA, 30 rue de St-Jean, P.O. Box 758, 1211 Geneva 13, Switzerland. Available online at http://www.ich.org/LOB/media/MEDIA423.pdf

[7] Available from U.S. Government Printing Office Superintendent of Documents, 732 N. Capitol St., NW, Mail Stop: SDE, Washington, DC 20401, http://www.access.gpo.gov.

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



Example infrared spectra are alternative presentations of an amorphous 100 % *d,l*-PLA homopolymer. (Spectra are courtesy of W. L. Gore & Associates, Inc., Flagstaff, AZ 86001, USA.)

FIG. 1 Poly(*d,l*-lactide) Resin Infrared Spectra

methylenechloride, or tetrahydrofuran at 20°C using a polarimetry method equal to or equivalent to the Optical Rotation procedure described within USP <781>.

5.4 *Molar Mass*:

5.4.1 The molar mass of the virgin polymer shall be indicated by inherent viscosity in dilute solution (IV). In addition to inherent viscosity (but not in place of), mass average molar mass and molar mass distributions maybe determined by gel permeation chromatography (GPC) according to Test Method D 3536 or D 3593, but using either chloroform or dichloromethane and polystyrene calibration standards.

5.4.2 Determine the inherent viscosity of the polymer preferentially in chloroform at 30°C using procedures similar to those described in Practice D 2857 and Test Method D 4603. Determination at a lower temperature of 25°C is allowable,