Designation: F 2313 – 03

Standard Specification for Virgin Poly(glycolide) and Poly(glycolide-co-lactide) Resins for Surgical Implants with Mole Fractions Greater Than or Equal to 70 % Glycolide[1]

This standard is issued under the fixed designation F 2313; 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 specification covers both virgin poly(glycolide) resin and poly(glycolide-co-lactide) resin with mole fractions greater than or equal to 70 % glycolide. This specification is not applicable to glycolide:lactide copolymers with mole fractions exceeding 30 % 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 and PGA:PLA resins for the hydrolytic byproducts to which they respectively degrade.

1.3 This specification addresses material characteristics of both virgin poly(glycolide) and poly(≥70 % glycolide-co-lactide) resins intended for use in surgical implants and does not apply to packaged and sterilized finished implants fabricated from this material.

1.4 As with any material, some characteristics may be altered by processing techniques (such as molding, extrusion, machining, assembly, sterilization, and so forth) 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 ensure safety and efficacy.

1.5 *This standard may suggest use of hazardous materials, operations, and equipment. This standard does not purport to address safety concerns associated with its use. It is the responsibility of the user of this standard to establish appropriate safety and health practices and to 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

D 2857 Practice for Dilute Solution Viscosity of Polymers

D 3536 Test Method for Molecular Weight Averages and Molecular Weight Distribution by Liquid 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]

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 Standards:*

United States Pharmacopeia (USP) Edition 26[4]

ISO 10993-9 Biological Evaluation of Medical Devices, Part 9: Framework for Identification and Quantification of Potential Degradation Products, Annex A[5]

21 CFR 820, United States Code of Federal Regulations, Title 21—Food and Drugs Services, Part 820—Quality System Regulation[6]

ANSI/ISO/ASQ Q9000-2000, Quality Management Systems; Fundamentals and Vocabulary[5]

ANSI/ISO/ASQ Q9001-2000, Quality Management Systems; Requirements[5]

3. Terminology

3.1 *Definitions:*

[1] This specification is under the jurisdiction of ASTM Committee F04 on Medical 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.

[4] Available from U.S. Pharmacopeia (USP), 12601 Twinbrook Pkwy., Rockville, MD 20852.

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

[6] Available from U.S. Government Printing Office Superintendent of Documents, 732 N. Capitol St., NW, Mail Stop: SDE, Washington, DC 20401.

3.1.1 *virgin polymer*, *n*—the form of poly(glycolide) or poly(glycolide-co-lactide) as synthesized from its monomers and prior to 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.

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 Polymers covered by this specification shall be composed either of glycolide, or of a combination of glycolide and lactide where the lactide content does not exceed 30 % (34.7 % by weight). To ensure 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(glycolide) homopolymer or poly(glycolide-co-lactide) 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 practices similar to those described in Practice E 1252. A typical infrared transmission reference spectrum for PGA homopolymer is shown in Fig. 1. A typical infrared transmission reference spectrum for a 90 % PGA:10 % l-PLA copolymer is shown in Fig. 2.

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

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

5.2.3.1 Identity of either poly(glycolide) homopolymer or poly(glycolide-co-lactide) copolymer may be confirmed through sample dissolution,^{1}H-NMR spectroscopy, and the use of a suitable reference spectrum. Sample dissolution is in deuterated hexafluoroisopropanol (D-HFIP) or other proton-free solvent able to fully solvate the specimen. 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 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(glycolide) homopolymer or poly(glycolide-co-lactide) 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 *Molecular Weight*:

5.3.1 The molecular 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), weight average molecular mass and molecular mass distributions may be determined by gel permeation chromatography (GPC) according to Test Methods D 3536 or D 3593, but using hexafluoroisopropanol (HFIP) solvent and poly methylmethacrylate (PMMA) calibration standards.

5.3.1.1 Determine the inherent viscosity of the polymer either in hexafluoroisopropanol (HFIP) or hexafluoroacetone sesquihydrate (HFAS) at 30°C using procedures similar to those described in Practice D 2857 and Test Method D 4603. Inherent viscosity is determined utilizing the following equation:

$$IV = \frac{ln\frac{t}{t_o}(v)}{w} \quad (1)$$

where:

IV = inherent viscosity (at 30°C in dl/gram),
t = efflux time in seconds for diluted solution,
t_o = efflux time in seconds for source solvent,
w = weight of polymer being diluted (in grams), and
v = dilution volume in deciliters (Note: 1 dl = 100 mL).

Resin concentration for IV analysis must be 0.5 % w/v or less, with resin analyte concentrations of 0.1 % w/v (that is, 0.001 g/ml or 1 mg/ml) recommended. When reporting results, identify the solvent utilized, analyte concentration, and analysis temperature.

5.4 *Residual Monomer*:

5.4.1 The virgin polymer shall have a combined total residual monomer content less than or equal to 2 % by weight.

5.4.1.1 Determine weight percent residual monomer by gas chromatography, ^{1}H-NMR spectroscopy (using D-HFIP or other proton-free solvent able to fully solvate the specimen), or other suitably sensitive analytic method as agreed upon by supplier and purchaser.

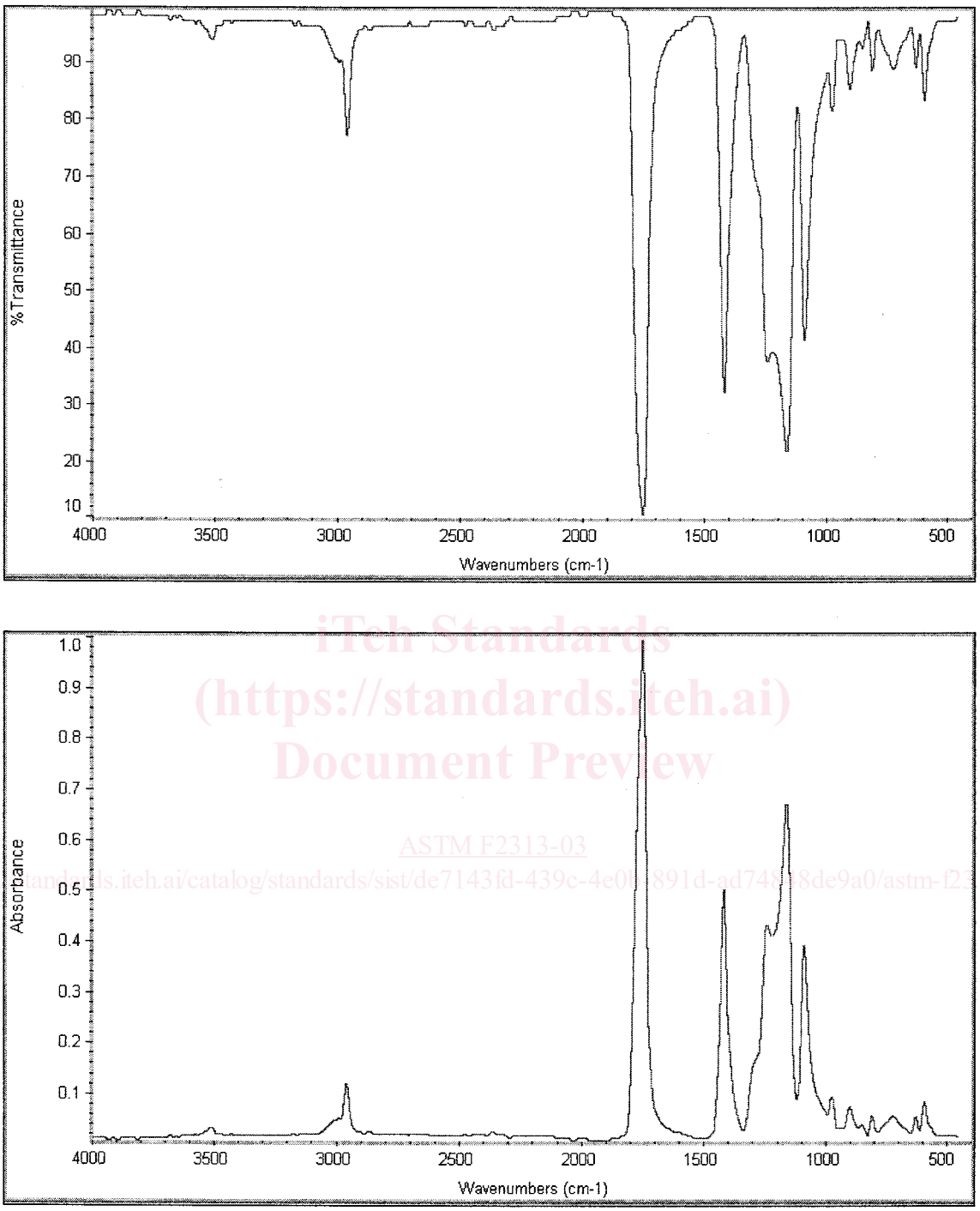
5.5 *Residual Solvents*:

5.5.1 If any solvent is utilized in any resin manufacturing or purification step, determine residual levels of any utilized solvent(s) by gas chromatography or other suitable method as agreed upon by supplier and purchaser. Acceptable residual levels of a solvent shall be reflective of toxicity, with a maximum acceptable level (regardless of toxicity) presented in Table 1.

5.6 *Heavy Metals*:

5.6.1 Determine residual Heavy Metals per Method II, Chapter 231 of U.S. Pharmacopeia.

5.6.2 Heavy Metals generally refers to divalent cations of the elements antimony (Sb), arsenic (As), cadmium (Cd), copper (Cu), mercury (Hg), and lead (Pb). Since stannous tin (Sn^{2+}) carries potential to influence test results, the amount ascertained by alternative analytic means (see below) to be directly attributable to tin in may be ignored, provided that the



NOTE—Supplied example infra-red spectrum is of "Dexon Medical Suture (beige)" as acquired from the Hummel Polymer Library, available from: Thermo Nicolet Corporation, 5225 Verona Road, Madison, WI 53711-4495, USA.

FIG. 1 Poly(glycolide) Resin Infrared Spectrum