Designation: F 1925 – 99ε1

Standard Specification for Virgin Poly(L-Lactic Acid) Resin for Surgical Implants[1]

This standard is issued under the fixed designation F 1925; 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—Figure 2 was editorially added in July 2001 because it had been inadvertently left out of the previous edition.

1. Scope

1.1 This specification covers virgin poly(L-lactic acid) resin (or abbreviated as PLLA resin) intended for use in surgical implants. This specification does not cover stereoisomeric compositions based on various D, L, or DL copolymer ratios.

1.2 This specification addresses material characteristics of virgin poly(L-lactic acid) resin and does not apply to packaged and sterilized finished implants fabricated from this material.

1.3 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 using those test methods which are appropriate to assure safety and efficacy.

1.4 The values stated in SI units are to be regarded as the 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:*

D 1505 Test Method for Density of Plastics by the Density-Gradient Technique[2]

D 1898 Practice for Sampling of Plastics[3]

D 2857 Practice for Dilute Solution Viscosity of Polymers[3]

D 3536 Test Method for Molecular Weight Averages and Molecular Weight Distribution by Liquid Exclusion Chromatography (Gel Permeation Chromatography - GPC)[4]

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[4]

D 3892 Practice for Packaging of Plastics[4]

F 748 Practice for Selecting Generic Biological Test Methods for Materials and Devices[5]

2.2 *ISO Standard:*

ISO/DIS 10993-9, Biological Evaluation of Medical Devices, Part 9 Degradation of Materials Related to Biological Testing, Annex A[6]

3. Terminology

3.1 *Definitions of Terms Specific to This Standard:*

3.1.1 *generic property*—that property which is determined solely by the chemical composition and structure of the virgin polymer

3.1.2 *virgin polymer*—the form of poly(L-lactic acid) as obtained from the manufacturer and before fabrication into a medical device.

4. Virgin Poly(L-Lactic Acid) Resin Requirements

4.1 *Generic Properties*:

4.1.1 The virgin polymer shall be a homopolymer of L-lactide with a density between 1.20 and 1.28 g/cm^3 (see 6.5 for evaluation method).

4.1.2 The molecular mass of the virgin polymer shall be indicated by relative solution viscosity in accordance with 6.2. In addition to solution 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.

4.1.3 The virgin polymer shall be identified as a polylactide by infrared or ^{1}H-NMR spectroscopy.

4.1.3.1 The virgin polymer shall yield an infrared spectrum which exhibits major absorption bands only at the wavelengths that appear in a suitable reference spectrum. A typical infrared transmission spectrum is shown in Fig. 1.

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

4.1.3.3 An infrared spectrum cannot distinguish between the different available stereoisomeric polylactic acids. It is used

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[2] *Annual Book of ASTM Standards*, Vol 08.01.

[3] *Annual Book of ASTM Standards*, Vol 08.02.

[4] *Annual Book of ASTM Standards*, Vol 08.03.

[5] *Annual Book of ASTM Standards*, Vol 13.01.

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

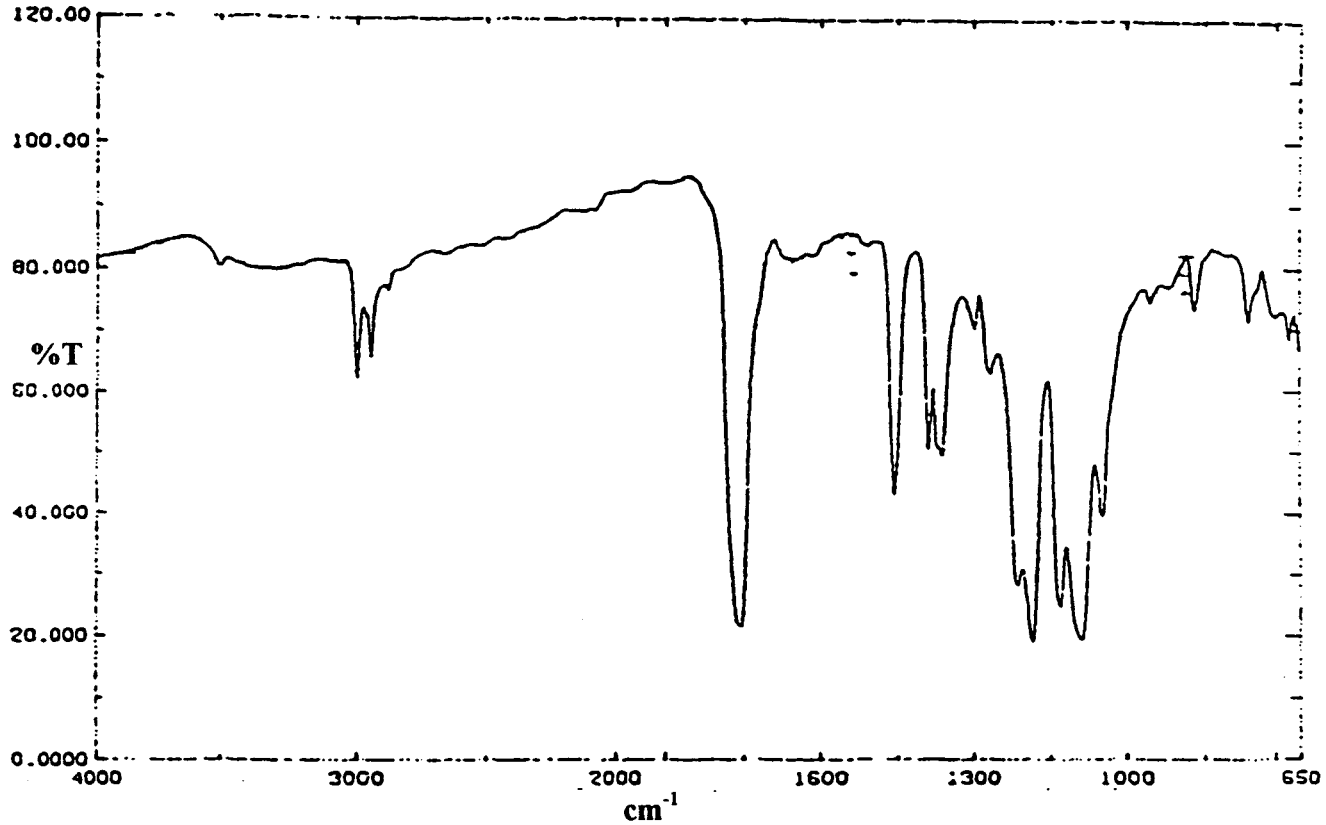

FIG. 1 Poly(L-Lactic Acid) Resin Infrared Spectrum

TABLE 1 Physical/Chemical Property Requirements of Virgin Poly(L-Lactic Acid) Resins

Analyte	Residual Solvent(s), (Total, %)	Residual Water, %	Residual Tin (Sn), ppm	Heavy Metals, (as Lead), ppm	Sulfated Ash, %
Requirement	≤0.01	≤0.5	≤200	≤300	≤0.1

here only as a means of identifying the material as a polylactide.

4.1.3.4 The virgin polymer shall yield a ^{1}H-NMR spectrum which exhibits major absorption bands only at the frequencies that appear in a suitable reference spectrum. A typical ^{1}H-NMR spectrum is shown in Fig. 2.

4.1.3.5 Additional absorption bands may be indicative of known, or unknown, impurities including residual solvents and monomers, and catalysts (refer to residual solvent, monomer, and tin (catalyst) limits specified in Table 1) and 4.1.5.

4.1.3.6 A ^{1}H-NMR spectrum cannot distinguish between the different available stereoisomeric polylactic acids. It is used here only as a means of identifying the material as a polylactide.

4.1.4 The virgin polymer shall have a specific optical rotation between −155 and −160° when measured as specified in 6.3.

4.1.5 The virgin polymer shall have a residual monomer content less than or equal to 2.0 % when assayed in accordance with 6.4. Virgin polymers having inherent viscosities greater than 2 dL/g and intended for injection molding or load-bearing applications shall not have a residual monomer content greater

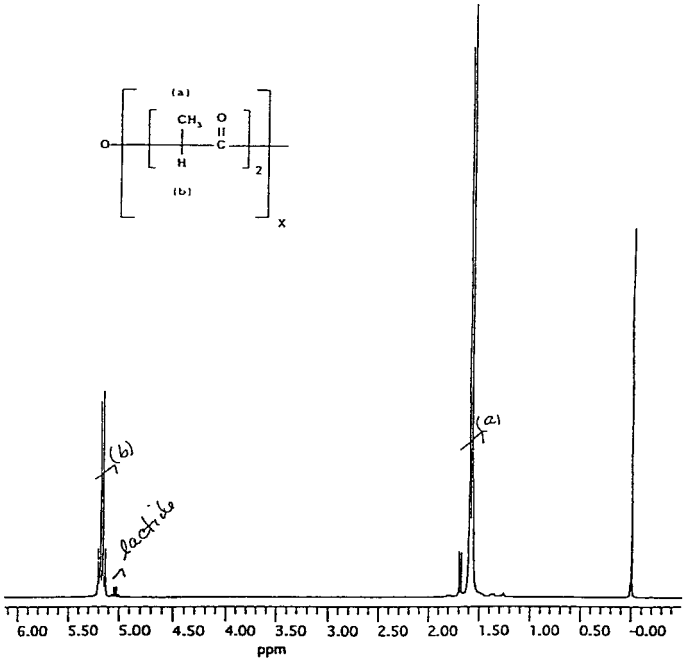

FIG. 2 Poly(L-Lactic Acid) Resin ^{1}H-NMR Spectrum

than 0.1 % when assayed in accordance with 6.3.

4.1.6 The virgin polymer shall have the chemical and physical properties as listed in Table 1 as determined by the methods listed in Section 6.

5. Sampling

5.1 Where applicable, the requirements of this specification

shall be determined for each lot of the virgin polymer by sampling sizes and procedures according to Practice D 1898.

6. Test Methods

6.1 Determine the density in accordance with Test Method D 1505.

6.2 Determine the relative solution viscosity in chloroform at 30°C using Practice D 2857.

6.3 Determine specific optical rotation in dichloromethane at 20°C in accordance with ISO/DIS 10993-9, Annex A.

6.4 Determine volume percent residual monomer by ^{1}H-NMR or gas chromatography or as agreed upon by supplier and purchaser.

6.5 Determine residual solvent(s) by gas chromatography or as agreed upon by supplier and purchaser.

6.6 Determine the amount of residual moisture (water) by Karl-Fischer titration, or as agreed upon by supplier and purchaser.

6.7 Determine the amount of residual tin (Sn) by atomic absorption/emission (AA) spectroscopy or inductively coupled plasma (ICP) spectroscopy.

6.8 Determine residual heavy metals as lead in accordance with Method 231 of U.S. Pharmacopeia[7].

6.9 Determine the sulfated ash content by ignition at 700°C, or as agreed upon by supplier and purchaser.

7. Packaging and Labeling

7.1 Packaging material shall meet the standards set forth in Practice D 3892.

8. Biocompatibility[8]

8.1 The suitability of these materials from a human implant perspective is dependent on the specific application. The biologic tests appropriate for the specific site, such as recommended in Practice F 748 should be used as a guideline.

8.2 No known surgical implant material has ever been shown to be completely free of adverse reactions in the human body. However, long-term clinical experience of use of specific compositions and formulations of this material class referred to in this standard has shown that an acceptable level of biological response can be expected, if the material is used to appropriate applications.

9. Keywords

9.1 PLLA; Poly(L-lactic acid); polylactide; virgin polymer

[7] Method 231 of U.S. Pharmacopeia, "Heavy Metals,", Edition XXII.

[8] Bergsma, J.E., de Bruijin, W.C., Rozema, F.R., Bos, R.R.M., and Boering, G., "Late Degradation Tissue Response to Poly(L-Lactide) Bone Plates and Screws," *Biomaterials*, 1995, pp. 16:25-31.

APPENDIX

(Nonmandatory Information)

X1. RATIONALE

X1.1 This standard material specification is written for PLLA resin and not for objects (for example, test samples or devices) fabricated from PLLA. The properties of objects fabricated from PLLA resin, such as mechanical properties, are dependent upon the processing conditions used during fabrication and thus fall outside of the scope of this PLLA resin standard. Properties in this standard are therefore specified only for PLLA resin and not for its fabricated form. Several potentially applicable ASTM standards are listed in Section 2, Referenced Documents, which may be followed to determine fabricated-form properties for devices and test samples fabricated from PLLA resin.

X1.2 PLLA resin may be synthesized with many different molecular weight ranges and distribution. Each such system will possess unique molecular weight dependent properties. Therefore certain physical, mechanical, and thermal properties (for example, glass transition, melt temperatures, and tensile properties) are not specified in this document.

X1.3 Most PLLA resin suppliers will provide analyses upon request relating to bioburden or pyrogens, or both. Bioburden is a measure of the number of viable cell colonies (aerobic, anaerobic, and spore cells) per gram of resin material. Pyrogen content is a measure of the presence of bacterial endotoxins which is commonly measured by the Limulus Amebocyte Lysate test (see 2.2). Because these properties may be significantly influenced by the exposure of the resin to any nonsterile environment, such properties are not required in this materials standard.

X1.4 While it is obviously ideal to have zero foreign particles within any bioabsorbable implant material, under practical processing conditions, it must be expected that processing related particles of foreign matter may be present to some degree. Unfortunately, at this time, there are no known published studies dealing with typical foreign particle levels in this resin material or their effect upon resin properties. Such a specification may be established in the future as information regarding this parameter is developed by methods such as round-robin use of this standard for selected samples of PLLA resin from various commercial sources.