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Standard Specification for Implantable Epoxy Electronic Encapsulants[1]

This standard is issued under the fixed designation F641; 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 thermoset plastics based on diglycidyl ethers of bisphenol A and amino functional curing agents or amine catalysts.

1.2 The epoxy encapsulants covered by this specification are intended to provide a tissue-compatible protective covering for implantable medical devices such as pulse generators, telemetry devices, and RF receivers. The biocompatibility of epoxy plastics has not been established. Epoxy plastic is a generic term relating to the class of polymers formed from epoxy resins, certain curing agents or catalysts, and various additives. Since many compositions and formulations fall under this category, it is essential that the fabricator ensure safety of implantability of the specific composition or formulation for the intended use by current state-of-the-art test methods. This specification can be used as a basis for standardized evaluation of biocompatibility for such implantable encapsulants.

1.3 The encapsulants covered by this specification are for use in devices intended as long-term implants.

1.4 *Limitations*—This specification covers only the initial qualification of epoxy encapsulants for implantable electronic circuitry. Some of the requirements are not applicable to routine lot-to-lot quality control.

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

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, health, and environmental practices and determine the applicability of regulatory limitations prior to use.*

1.7 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.*

2. Referenced Documents

2.1 *ASTM Standards:*[2]

D149 Test Method for Dielectric Breakdown Voltage and Dielectric Strength of Solid Electrical Insulating Materials at Commercial Power Frequencies

D150 Test Methods for AC Loss Characteristics and Permittivity (Dielectric Constant) of Solid Electrical Insulation

D257 Test Methods for DC Resistance or Conductance of Insulating Materials

D570 Test Method for Water Absorption of Plastics

D638 Test Method for Tensile Properties of Plastics

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

D1042 Test Method for Linear Dimensional Changes of Plastics Caused by Exposure to Heat and Moisture

D1239 Test Method for Resistance of Plastic Films to Extraction by Chemicals

D1434 Test Method for Determining Gas Permeability Characteristics of Plastic Film and Sheeting

D2240 Test Method for Rubber Property—Durometer Hardness

D2471 Practice for Gel Time and Peak Exothermic Temperature of Reacting Thermosetting Resins (Withdrawn 2008)[3]

D2562 Practice for Classifying Visual Defects in Parts Molded from Reinforced Thermosetting Plastics

D2566 Test Method for Linear Shrinkage of Cured Thermosetting Casting Resins During Cure (Withdrawn 1993)[3]

D2734 Test Methods for Void Content of Reinforced Plastics

D3137 Test Method for Rubber Property—Hydrolytic Stability

F74 Practice for Determining Hydrolytic Stability of Plastic Encapsulants for Electronic Devices (Withdrawn 1994)[3]

F135 Test Method for Embedment Stress Caused by Casting

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

Compounds on Glass-Encased Electronic (Withdrawn 1997)[3]
F602 Criteria for Implantable Thermoset Epoxy Plastics
F748 Practice for Selecting Generic Biological Test Methods for Materials and Devices
F895 Test Method for Agar Diffusion Cell Culture Screening for Cytotoxicity
F981 Practice for Assessment of Compatibility of Biomaterials for Surgical Implants with Respect to Effect of Materials on Muscle and Insertion into Bone

2.2 *AAMI Standard:*[4]
EOS-D E-O Sterilization Standard

2.3 *ISO Standard:*[5]
ISO 10993 Biological Evaluation of Medical Devices

3. Classification

3.1 Encapsulants shall be classified as follows:

3.1.1 *Type I*—Those encapsulants which contact the tissue directly or indirectly.

3.1.2 *Type II*—Those encapsulants used only within hermetically sealed containers. The epoxy encapsulant has no contact with tissues or physiological fluids.

4. Chemical Composition

4.1 *Additives* (Type I Encapsulants Only):

4.1.1 *Reactive Diluents*—The following compounds when used as reactive diluents shall not be used in concentrations greater than 12 parts per hundred resin (phr).

4.1.1.1 Butyl glycidyl ether (BGE).

4.1.1.2 Phenyl glycidyl ether (PGE).

4.1.2 *Other Additives* (see Note 1)—Other additives shall be shown to be nonextractable in 37 °C physiological saline for the device design life in concentrations sufficient to significantly affect the properties of the encapsulant or to produce a significant biological reaction.

NOTE 1—Other additives, as indicated in Criteria F602, include compounds such as nonreactive diluents, fillers, release agents, and the like.

4.1.3 *Phthalate Esters*—Phthalate esters such as dibutyl phthalate shall not be used in concentrations ≥10 phr.

4.2 *Mix Ratios* (Type I and Type II Encapsulants):

4.2.1 *Amines*—The mix ratio shall be maintained at ±5 equivalent % of stoichiometry.

4.2.2 *Catalysts*—The mix ratio shall be maintained within the ranges recommended by the formulator.

4.3 *Carbonates* (Type I and Type II Encapsulants)—The encapsulant shall be poured under conditions such that the formation of amine carbonates is minimized. The device manufacturer may specify maximum limits for carbon dioxide or water vapor, or both, in the atmosphere in which the encapsulant is being mixed or poured.

5. Physical Properties

5.1 *Type I Encapsulants:*

5.1.1 *Peak Exotherm Temperature* (Practice D2471)—The peak exotherm temperature during cure shall be kept below the maximum acceptable value for the lowest temperature rated component of the device.

5.1.2 *Fully Cured Specimens*—The required properties measured on fully cured specimens conditioned as in 6.1 are as follows:

5.1.2.1 *Transparency*—In cases where no fillers or reinforcements are used, the encapsulant shall have sufficient transparency so that the circuitry may be visually inspected after encapsulation.

5.1.2.2 *Foreign Particles*—No foreign particles, particulate matter, or gross contamination shall be observed when checked under 2× wide field magnification.

5.1.2.3 *Biocompatibility Testing*—While cell culture methods as described in Test Method F895 may be appropriate for the lot-to-lot screening of fully cured specimens, the basic recipe used should have been qualified for its overall tissue response by methods such as those suggested in Practice F748 or ISO 10993 for the intended application, including testing according to Practice F981.

(1) Biocompatibility testing should be performed on specimens that have been processed and sterilized per the methods intended for the final device.

5.1.2.4 USP Bacterial Endotoxin Test[6] or other Pyrogen methods which have been demonstrated to be of equal or greater sensitivity—Pass.

5.1.2.5 *Sterilant Residues* (AAMI EOS-D)—Where applicable, the concentration of ethylene oxide, ethylene chlorohydrin, ethylene glycol, and dichlorodifluoromethane (or the equivalents) at the time of implantation shall be shown to be within safe limits prescribed by the device manufacturer.

5.1.2.6 The cure shrinkage (Test Method D2566) or embedment stress (Test Method F135) shall be ≤2 %. The stress shall not exceed the limits of the most pressure-sensitive components.

5.1.2.7 Tissue Culture Test (Agar Overlay)[7] or Test Method F895—Pass.

5.1.3 *Required Cured Properties Measured in Long-Term Immersion Tests for Type I Encapsulants*—The property values prescribed in Table 1 shall be obtained at 22 ± 3 °C and 50 ± 10 % relative humidity on specimens conditioned as in 6.3. Samples shall be wiped dry prior to test with a lint-free tissue, as appropriate.

5.1.4 Optional cured properties measured after accelerated immersion for Type I encapsulants may be determined for screening purposes after conditioning as in 6.2.

5.2 *Type II Encapsulants:*

5.2.1 *Peak Exotherm Temperature* (Practice D2471)—The peak exotherm temperature during cure shall be kept below the

[4] Available from Association for Advancement of Medical Instrumentation, 1500 Wilson Blvd., Suite 417, Arlington, VA 22209.

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

[6] *U.S. Pharmacopeia*, USP-NF, <85>, available from U.S. Pharmacopeia (USP), 12601 Twinbrook Pkwy., Rockville, MD 20852-1790, http://www.usp.org.

[7] Guess, W. L., et al., *Journal of Pharmaceutical Sciences*, Vol 54, 1965, pp. 1545–1547.

TABLE 1 Cure Requirements for Long-Term Immersion Tests for Type I Encapsulants

Property	Requirement	ASTM Method
Extraction	<1 % in water	D1239
Water absorption	≤4 %	D570
Dielectric strength	>11.8 kV/mm	D149
Dielectric constant	>2.0	D150
Dissipation factor	<0.05	D150
Elongation	>1.5 %	D638
Flexural strength	≥1380 MPa	D790
Gas permeation	[A]	D1434
Hardness	≥60 Shore D	D2240
Dimensional stability	<0.5 % change	D1042
Tangent modulus	≥1380 MPa	D638
Tensile strength (with outgassing power sources)	≥55 MPa	D638
Tensile strength (without outgassing power sources)	≥7 MPa	D638
Visual defects	none that adversely affect the safety, efficacy, or reliability of the device	D2562
Voids	none that adversely affect the safety, efficacy, or reliability of the device	D2734
Volume resistivity	10^{10} Ω·cm	D257

[A] For those devices containing gas-evolving power sources, the hydrogen permeation coefficient shall be 1.18×10^{-3} [(STP)(cm^3)(mm)/(atm)(day)(cm^2)]; or the encapsulant shall allow the escape of 0.06 cm^3 of hydrogen per cell day; or provision shall be made to ensure that gaseous material evolving from the power sources will be adequately disposed of in such a manner that the encapsulant is not comprised.

maximum acceptable value for the lowest temperature rated component of the device.

5.2.2 The property values prescribed in Table 2 shall be determined at 22 ± 3 °C and 50 ± 10 % relative humidity on fully cured samples conditioned as in 6.1.

6. Specimen Preparation

6.1 *Preparation*—Prepare specimens used for evaluation of properties of the cured material in the same manner as the intended product. Such conditioning shall include all specified relevant variables for the product prior to implantation, including specimen size or shape, cure time, cure temperature, post-cure, cleaning, packaging, sterilization, and aeration.

6.2 *Accelerated Immersion:*

6.2.1 For screening purposes, immerse specimens prepared as in 6.1 in refluxing physiological saline of pH 7.4 ± 0.2 for seven days.

6.2.2 Prior to evaluation, allow the specimens to equilibrate to the test temperature of 22 ± 3 °C in physiological saline of pH 7.4 ± 0.2.

6.2.3 Condition one set of controls at 100 ± 3 °C and another set at 22 ± 3 °C for seven days at 50 ± 10 % relative humidity.

6.2.4 Since two variables, heat and moisture, are inherent in this test, data from specimens refluxed seven days in saline may be compared to controls conditioned dry at 100 °C and at 22 °C. Thus, one may estimate the long-term effects of moisture as opposed to the effects of moisture and heat or heat alone.

6.3 *Long-Term Immersion* (Test Method D3137 or Practice F74):

6.3.1 Prepare the specimens in accordance with 6.1.

6.3.2 During initial qualification of the formulation, immerse specimens in 37 ± 3 °C aerated physiological saline of pH 7.4 ± 0.2 with periodic sampling for evaluation as is appropriate for a period of time consistent with projected service life. Immersion shall continue for the projected service life of the device. For devices intended for long-term implant, however, it may not be practical to complete tank tests over the device's projected service life before one can claim compliance with the specification. One shall be considered in compliance with this section of the specification, therefore, if specimens meet the requirements of 5.4 after one year's immersion.

6.3.3 Store controls at 22 ± 3 °C and 50 ± 10 % relative humidity.

7. Inspection

7.1 As a minimum, the following methods shall be used to characterize the formulation prior to mixing:

7.1.1 Infrared spectroscopy on each component.

7.1.2 Amine number on curing agent.

7.1.3 Epoxide equivalent weight on resin.

TABLE 2 Cure Requirements for Long-Term Immersion Tests for Type II Encapsulants

Property	Requirement	ASTM Method
Foreign particles	none visible	...
Cure shrinkage or embedment stress	≤2 %	D2566 or F135, respectively
Dielectric constant	>2.0	D150
Dielectric strength	>11.8 kV/mm	D149
Dissipation factor	<0.05	D150
Dimensional stability	<0.5 % change	D1042
Visual defects	none that adversely affect the safety, efficacy, or reliability of the device	D2562
Voids	none that adversely affect the safety, efficacy, or reliability of the device	D2734
Volume resistivity	10^{10} Ω·cm	D257