Designation: F3225 – 17 (Reapproved 2022)

Standard Guide for Characterization and Assessment of Vascular Graft Tissue Engineered Medical Products (TEMPs)[1]

This standard is issued under the fixed designation F3225; 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 guide is intended as a resource for individuals and organizations involved in the development, production, delivery, and regulation of tissue engineered medical products (TEMPs) intended for use in the surgical repair, replacement, shunting, and/or bypass of blood vessels. This guide is intended for use related to the *in vitro* assessment of TEMP vascular grafts. *In vitro* cellular characterization and *in vivo* testing are not within scope for this standard guide.

1.2 *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.*

1.3 *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]

F1635 Test Method for ***in vitro*** Degradation Testing of Hydrolytically Degradable Polymer Resins and Fabricated Forms for Surgical Implants

F2150 Guide for Characterization and Testing of Biomaterial Scaffolds Used in Regenerative Medicine and Tissue-Engineered Medical Products

F2210 Guide for Processing Cells, Tissues, and Organs for Use in Tissue Engineered Medical Products (Withdrawn 2015)[3]

F2211 Classification for Tissue-Engineered Medical Products (TEMPs)

F2212 Guide for Characterization of Type I Collagen as Starting Material for Surgical Implants and Substrates for Tissue Engineered Medical Products (TEMPs)

F2312 Terminology Relating to Tissue Engineered Medical Products

F2382 Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)

F2739 Guide for Quantifying Cell Viability and Related Attributes within Biomaterial Scaffolds

STP 997-EB Compositional Analysis by Thermogravimetry

2.2 *US FDA Regulations and Guidance Documents:*[4]

21 CFR 610.12 General Biological Products Standards—Sterility

21 CFR 1270 Human Tissue Intended for Transplantation

21 CFR 1271 Human Cells, Tissues, and Cellular and Tissue-Based Products

FDA Guidance for Industry Pyrogen and Endotoxins Testing: Questions and Answers

Guidance for Industry Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps)

FDA Guidance for Industry Container and Closure System Integrity Testing *in Lieu* of Sterility Testing as a Component of the Stability Protocol for Sterile Products

Guidance for Industry and Food and Drug Administration Staff Use of International Standard ISO-10993-1, Biological Evaluation of Medical Devices—Part 1: Evaluation and testing within a risk management process

[1] This guide is under the jurisdiction of ASTM Committee F04 on Medical and Surgical Materials and Devices and is the direct responsibility of Subcommittee F04.44 on Assessment for TEMPs.

Current edition approved Sept. 1, 2022. Published September 2022. Originally approved in 2017. Last previous edition approved in 2017 as F3225 – 17. DOI: 10.1520/F3225-17R22.

[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.

[4] Available from U.S. Government Printing Office, Superintendent of Documents, 732 N. Capitol St., NW, Washington, DC 20401-0001, http://www.access.gpo.gov.

2.3 *ISO Standards:*[5]

ISO 7198 Cardiovascular implants and extracorporeal systems—Vascular prostheses—Tubular vascular grafts and vascular patches

ISO 10993 Biological evaluation of medical devices

ISO 11135 Sterilization of health-care products—Ethylene oxide—Requirements for the development, validation and routine control of a sterilization process for medical devices

ISO 11137 (Parts 1, 2 and 3) Sterilization of health care products – Radiation

ISO 11737-1 Sterilization of medical devices—Microbiological methods—Part 1: Determination of a population of microorganisms on products

ISO 11737-2 Sterilization of medical devices—Microbiological methods—Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process

ISO 22442-1 Medical devices utilizing animal tissues and their derivatives—Part 1: Application of risk management

ISO 22442-3 Medical devices utilizing animal tissues and their derivatives—Part 3: Validation of the elimination and/or inactivation of viruses and transmissible spongiform encephalopathy (TSE) agents

2.4 *Other Documents:*

United States Pharmacopeia XXVII <71> Sterility Tests

ICH Harmonized Tripartite Guideline Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Q5A(R1)

American Association of Tissue Banks (AATB) AATB Standards for Tissue Banking

ANSI/AAMI ST72 Bacterial Endotoxins—Test Methods, Routine Monitoring, and Alternative to Batch Testing

3. Summary of Guide

3.1 It is the intent of this guide to provide a compendium of information that may be related to the functional characteristics of vascular graft TEMPs intended to surgically replace, bypass, or form shunts between sections of the vascular system. Examples of functional characteristics include vasoactivity and mechanical properties (e.g., burst pressure, tensile strength, creep) suitable for implantation. TEMPs may be composed of biological products (e.g., cells, organs, tissues, and processed biologics), biomaterials (e.g., substrates and scaffolds composed of polymers or extracellular matrix (ECM) components such as collagen), and/or biomolecules (e.g., recombinant proteins) (see Terminology F2312). Examples of TEMPs are listed in Classification F2211.

3.2 ISO 7198 provides basic requirements for sterile vascular prostheses and the methods of testing which will enable evaluation of vascular prostheses. The degree of sterility (sterility assurance level of 1×10^{-3} versus 1×10^{-6}) will be determined by the materials of construction and their ability to be sterilized without compromising their function once implanted.

[5] Available from International Organization for Standardization (ISO), ISO Central Secretariat, BIBC II, Chemin de Blandonnet 8, CP 401, 1214 Vernier, Geneva, Switzerland, http://www.iso.org.

3.3 Throughout this guide, the reader is referred to other documents that may provide specific information that can be applied in the manufacture and testing of TEMPs. Although many of these documents were not written with TEMPs in mind, parts are often applicable. Most of the potentially applicable position papers and guidance documents from many regions of the world can be accessed via the internet. New documents are continually produced, and existing documents are continually updated.

3.4 The application of this guide does not guarantee clinical success of a finished product, but will help develop and characterize a given vascular graft TEMP developed for the purpose of surgically replacing, bypassing, or forming shunts between sections of the vascular system.

3.5 This guide does not suggest that all listed tests be conducted. The decision regarding applicability or suitability of any particular test method remains the responsibility of the supplier, user, or regulator of the material based on risk, applicable regulations, characterizations, and preclinical/clinical testing.

4. Significance and Use

4.1 A common therapy to mitigate the pathological effects of blood vessel occlusion or aneurysm-related vascular wall weakening is to reroute blood flow around the diseased vascular regions. Autologous and non-autologous grafts are often used as vascular substitutes surgically to achieve this therapeutic intervention. Vascular graft TEMPs may also be used for these purposes. They may also be used to create or revise arteriovenous shunts.

4.2 Coronary, carotid, renal, common iliac, external iliac, superficial femoral, and popliteal arteries are examples of vascular sites commonly requiring bypass surgery.

4.3 TEMPs may be composed of biological products (for example, cells, organs, and tissues), biomaterials (for example, substrates and scaffolds composed of polymers or collagen), biomolecules (for example, recombinant proteins, native/biological proteins, amino acids, peptides, fatty acids, sugars, and other macromolecules), and various combinations thereof (see Terminology F2312). Examples of TEMPs are listed in Classification F2211.

4.4 TEMPs may be used with the intent of facilitating the surgical outcome by improving the biological repair and/or reconstruction, by accommodating the mechanical loads at the repair site, or by a combination of these mechanisms.

4.5 Clinical evidence of improved surgical outcomes may include patency, reduced incidence of revision surgery, reduced rate of implant infection, and improved functionality after surgery.

5. Synthetic Biomaterials

5.1 *Polymer Types*—The biomaterial used may be formed from synthetic polymers, should elicit an acceptable biological response with minimal toxicity, and may be degradable or non-degradable. Examples of degradable polymers are glycolide, lactide, trimethylene carbonate, dioxanone,