Designation: F3666 – 25

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

This standard is issued under the fixed designation F3666; 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 repair and/or replacement of heart valves. This guide is intended for use related to the *in vitro* assessment of TEMP heart valves.

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

F2052 Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment

F2119 Test Method for Evaluation of MR Image Artifacts from Passive Implants

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

F2182 Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging

F2210 Guide for Processing Cells, Tissues, and Organs for Use in Tissue Engineered Medical Products (Withdrawn 2015)[3]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

F2213 Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment

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)

F2503 Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment

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

F2997 Practice for Quantification of Calcium Deposits in Osteogenic Culture of Progenitor Cells Using Fluorescent Image Analysis

F3354 Guide for Evaluating Extracellular Matrix Decellularization Processes

F3510 Guide for Characterizing Fiber-Based Constructs for Tissue-Engineered Medical Products

2.2 *Code of Federal 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

[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.

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[2] For referenced ASTM standards, visit the ASTM website, www.astm.org, or contact ASTM Customer Service at www.astm.org/contact. 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 Publishing Office (GPO), 732 N. Capitol St., NW, Washington, DC 20401, http://www.gpo.gov.

FDA 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
FDA Guidance for Industry Use of International Standard ISO 10993-1, Biological Evaluation of Medical Devices—Part 1: Evaluation and testing within a risk management process
FDA Guidance for Industry Testing and Labeling Medical Devices for Safety in the Magnetic Resonance (MR) Environment
FDA Guidance for Industry Reporting of Computational Modeling Studies in Medical Device Submissions

2.3 *ISO Standards:*[5]

ISO 10974 Assessment of the safety of magnetic resonance imaging for patients with an active implantable medical device
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 11137-1 Sterilization of health care products—Radiation—Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices
ISO 11137-2 Sterilization of health care products—Radiation—Part 2: Establishing the sterilization dose
ISO 11137-3 Sterilization of health care products—Radiation—Part 3: Guidance on dosimetric aspects of development, validation and routine control
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 20404 Biotechnology—Bioprocessing—General requirements for the design of packaging to contain cells for therapeutic use
ISO 21560 General requirements of tissue-engineered medical products
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
ISO 23033 Biotechnology—Analytical Methods—General requirements and considerations for the testing and characterization of cellular therapeutic products
ISO 5840-1 Cardiovascular Implants—Cardiac valve prostheses—Part 1: General requirements
ISO 5840-2 Cardiovascular Implants—Cardiac valve prostheses—Part 2: Surgically implanted heart valve substitutes
ISO 5840-3 Cardiovascular Implants—Cardiac valve prostheses—Part 3: Heart valve substitutes implanted by transcatheter techniques

2.4 *Other Documents:*

ANSI/AAMI ST72 Bacterial Endotoxins—Test Methods, Routine Monitoring, and Alternative to Batch Testing[6]
ICH Q5A(R1) Harmonized Tripartite Guideline—Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin[7]

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 the heart valve TEMPs used for the replacement of a natural heart valve. TEMPs may be composed of biological products (for example, cells, organs, tissues, and processed biologics), biomaterials (for example, substrates and scaffolds composed of polymers or extracellular matrix (ECM) components such as collagen), and/or biomolecules (for example, recombinant proteins; see Terminology F2312). Examples of TEMPs are listed in Classification F2211.

3.2 ISO 5840 provides basic requirements for all devices intended for implantation in the human heart as a heart valve and the methods of test which will enable evaluation of heart valve substitutes.

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.

3.4 The application of this guide does not guarantee clinical success of a finished product but will help to ensure consistency in the properties and characterization of a given heart valve TEMP.

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 product. The selection of tests should be based on the risk factors identified for a particular TEMP and its indication, within the context of applicable regulations, existing characterization data, and evidence from any preclinical and clinical testing.

4. Significance and Use

4.1 Valve replacement procedures due to valvular heart disease are performed annually as a result of structural

[5] Available from American National Standards Institute (ANSI), 1180 Avenue of the Americas, 10th Floor, New York, NY 10036, http://www.ansi.org.

[6] Available from American National Standards Institute (ANSI), 1180 Avenue of the Americas, 10th Floor, New York, NY 10036, http://www.ansi.org.

[7] Available from International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), ICH Secretariat, Route de Pré-Bois, 20, P.O Box 1894, 1215 Geneva, Switzerland, https://www.ich.org.