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Standard Guide for Design and Evaluation of Primary Flexible Packaging for Medical Products[1]

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1. Scope

1.1 This guide provides directions for the design and evaluation of primary flexible packages for medical products. The package materials must be selected appropriately for manufacturing process, end use, and the product being packaged.

1.2 This guide provides a compendium of test methods, practices, and procedures. Specific individual test methods must be selected based on the pertinent characteristics of the specific product to be packaged and the purpose for testing, research and development, or compliance. Not all test methods will be applicable.

1.3 This guide does not address acceptability criteria, which need to be determined jointly by the package producer and the medical products manufacturer.

1.4 This guide does not assess the product to be packaged or the sterilization method to be used.

1.5 The units cited in the referenced standard should be used.

2. Referenced Documents

2.1 *ASTM Standards:*[2]

D374 Test Methods for Thickness of Solid Electrical Insulation (Withdrawn 2013)[3]
D589 Test Method for Opacity of Paper (15° Diffuse Illuminant *A*, 89 % Reflectance Backing and Paper Backing) (Withdrawn 2010)[3]
D638 Test Method for Tensile Properties of Plastics
D645/D645M Test Method for Thickness of Paper and Paperboard (Withdrawn 2010)[3]
D726 Test Method for Resistance of Nonporous Paper to Passage of Air (Withdrawn 2009)[3]
D882 Test Method for Tensile Properties of Thin Plastic Sheeting
D1003 Test Method for Haze and Luminous Transmittance of Transparent Plastics
D1434 Test Method for Determining Gas Permeability Characteristics of Plastic Film and Sheeting
D1709 Test Methods for Impact Resistance of Plastic Film by the Free-Falling Dart Method
D1777 Test Method for Thickness of Textile Materials
D1894 Test Method for Static and Kinetic Coefficients of Friction of Plastic Film and Sheeting
D1922 Test Method for Propagation Tear Resistance of Plastic Film and Thin Sheeting by Pendulum Method
D1938 Test Method for Tear-Propagation Resistance (Trouser Tear) of Plastic Film and Thin Sheeting by a Single-Tear Method
D2019 Test Method for Dirt in Paper and Paperboard (Withdrawn 2010)[3]
D2457 Test Method for Specular Gloss of Plastic Films and Solid Plastics
D3078 Test Method for Determination of Leaks in Flexible Packaging by Bubble Emission
D3079 Test Method for Water Vapor Transmission of Flexible Heat-Sealed Packages for Dry Products
D3335 Test Method for Low Concentrations of Lead, Cadmium, and Cobalt in Paint by Atomic Absorption Spectroscopy
D3420 Test Method for Pendulum Impact Resistance of Plastic Film
D3718 Test Method for Low Concentrations of Chromium in Paint by Atomic Absorption Spectroscopy
D3776 Test Methods for Mass Per Unit Area (Weight) of Fabric

[1] This guide is under the jurisdiction of ASTM Committee F02 on Flexible Barrier Packaging and is the direct responsibility of Subcommittee F02.50 on Package Design and Development.

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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.

D3985 Test Method for Oxygen Gas Transmission Rate Through Plastic Film and Sheeting Using a Coulometric Sensor
D4169 Practice for Performance Testing of Shipping Containers and Systems
D4279 Test Methods for Water Vapor Transmission of Shipping Containers—Constant and Cycle Methods
D4321 Test Method for Package Yield of Plastic Film
D4332 Practice for Conditioning Containers, Packages, or Packaging Components for Testing
D4754 Test Method for Two-Sided Liquid Extraction of Plastic Materials Using FDA Migration Cell
D5264 Practice for Abrasion Resistance of Printed Materials by the Sutherland Rub Tester
D7386 Practice for Performance Testing of Packages for Single Parcel Delivery Systems
E398 Test Method for Water Vapor Transmission Rate of Sheet Materials Using Dynamic Relative Humidity Measurement
F17 Terminology Relating to Flexible Barrier Packaging
F88 Test Method for Seal Strength of Flexible Barrier Materials
F99 Guide for Writing a Specification for Flexible Barrier Rollstock Materials
F151 Test Method for Residual Solvents in Flexible Barrier Materials (Withdrawn 2004)[3]
F372 Test Method for Water Vapor Transmission Rate of Flexible Barrier Materials Using an Infrared Detection Technique (Withdrawn 2009)[3]
F392 Test Method for Flex Durability of Flexible Barrier Materials
F748 Practice for Selecting Generic Biological Test Methods for Materials and Devices
F813 Practice for Direct Contact Cell Culture Evaluation of Materials for Medical Devices
F895 Test Method for Agar Diffusion Cell Culture Screening for Cytotoxicity
F904 Test Method for Comparison of Bond Strength or Ply Adhesion of Similar Laminates Made from Flexible Materials
F1140 Test Methods for Internal Pressurization Failure Resistance of Unrestrained Packages
F1249 Test Method for Water Vapor Transmission Rate Through Plastic Film and Sheeting Using a Modulated Infrared Sensor
F1306 Test Method for Slow Rate Penetration Resistance of Flexible Barrier Films and Laminates
F1307 Test Method for Oxygen Transmission Rate Through Dry Packages Using a Coulometric Sensor
F1443 Practice for Using 0.008-in. (0.203-mm) Aperture Reflectometers as Test Instruments for Measuring Visual Image Quality of Business Copy Images
F1608 Test Method for Microbial Ranking of Porous Packaging Materials (Exposure Chamber Method)
F1884 Test Methods for Determining Residual Solvents in Packaging Materials
F1886 Test Method for Determining Integrity of Seals for Medical Packaging by Visual Inspection
F1921 Test Methods for Hot Seal Strength (Hot Tack) of Thermoplastic Polymers and Blends Comprising the Sealing Surfaces of Flexible Webs
F1927 Test Method for Determination of Oxygen Gas Transmission Rate, Permeability and Permeance at Controlled Relative Humidity Through Barrier Materials Using a Coulometric Detector
F1929 Test Method for Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration
F1980 Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices
F2029 Practices for Making Heatseals for Determination of Heatsealability of Flexible Webs as Measured by Seal Strength
F2054 Test Method for Burst Testing of Flexible Package Seals Using Internal Air Pressurization Within Restraining Plates
F2095 Test Methods for Pressure Decay Leak Test for Flexible Packages With and Without Restraining Plates
F2096 Test Method for Detecting Gross Leaks in Packaging by Internal Pressurization (Bubble Test)
F2203 Test Method for Linear Measurement Using Precision Steel Rule
F2217 Practice for Coating/Adhesive Weight Determination
F2250 Practice for Evaluation of Chemical Resistance of Printed Inks and Coatings on Flexible Packaging Materials
F2251 Test Method for Thickness Measurement of Flexible Packaging Material
F2252 Practice for Evaluating Ink or Coating Adhesion to Flexible Packaging Materials Using Tape
F2227 Test Method for Non-Destructive Detection of Leaks in Non-sealed and Empty Packaging Trays by CO_2 Tracer Gas Method
F2228 Test Method for Non-Destructive Detection of Leaks in Packaging Which Incorporates Porous Barrier Material by CO_2 Tracer Gas Method
F2338 Test Method for Nondestructive Detection of Leaks in Packages by Vacuum Decay Method
F2391 Test Method for Measuring Package and Seal Integrity Using Helium as the Tracer Gas
F2475 Guide for Biocompatibility Evaluation of Medical Device Packaging Materials
F2476 Test Method for the Determination of Carbon Dioxide Gas Transmission Rate (CO_2TR) Through Barrier Materials Using An Infrared Detector
F2559 Guide for Writing a Specification for Sterilizable Peel Pouches
F2622 Test Method for Oxygen Gas Transmission Rate Through Plastic Film and Sheeting Using Various Sensors
F2638 Test Method for Using Aerosol Filtration for Measuring the Performance of Porous Packaging Materials as a Surrogate Microbial Barrier
F2714 Test Method for Oxygen Headspace Analysis of Packages Using Fluorescent Decay

F2824 Test Method for Mechanical Seal Strength Testing for Round Cups and Bowl Containers with Flexible Peelable Lids
F2825 Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery
F2981 Test Method for Verifying Nonporous Flexible Barrier Material Resistance to the Passage of Air
F3004 Test Method for Evaluation of Seal Quality and Integrity Using Airborne Ultrasound
F3039 Test Method for Detecting Leaks in Nonporous Packaging or Flexible Barrier Materials by Dye Penetration
F3136 Test Method for Oxygen Gas Transmission Rate through Plastic Film and Sheeting using a Dynamic Accumulation Method

2.2 *EN/ISO Standards:*[4]
EN 868/1 Annex C Gurley, Schopper, Dye Penetration
ISO 2556 Plastics—Determination of Gas Transmission Rate of Films and Thin Sheets Under Atmospheric Pressure—Manometric Method
ISO 5636–5 Paper and Board—Determination of Air Permeance (Medium Range)—Part 5: Gurley Method
ISO 10993 Biological Evaluation of Medical Devices
ISO 11607–1 Packaging for Terminally Sterilized Medical Devices, Annex C
ISO 15105–1 Plastics—Film and Sheeting—Determination of Gas Transmission Rate—Part 1: Differential-Pressure Method
ISO 15105–2 Plastics—Film and Sheeting—Determination of Gas Transmission Rate—Part 2: Equal-Pressure Method

2.3 *Military Specification:*[5]
Mil Spec 36954C Bacterial Filtration Efficiency

2.4 *TAPPI Standards:*[6]
TAPPI T 404 Tensile Breaking Strength and Elongation of Paper and Paperboard
TAPPI T 437 Dirt in Paper and Paperboard
TAPPI T 460 Air Resistance of Paper (Gurley Method)
TAPPI T 494 Tensile Breaking Properties of Paper and Paperboard (Using Constant Rate of Elongation Apparatus)
TAPPI T 536 Resistance of Paper to Passage of Air (High Pressure Gurley Method)
TAPPI T 547 Air Permeance of Paper and Paperboard (Sheffield Method)

2.5 *ISTA Procedures:*[7]
ISTA 3A Packaged Products for Parcel Delivery System Shipments 70 kg (150 lb) or Less (standard, small, flat, or elongated)
ISTA 3E Unitized Loads of Same Product
ISTA 4AB Packaged-Products for Shipment in Known Distribution Channels
ISTA 6–FEDEX-A FedEx Procedures for Testing Packaged Products Weighing Up to 150 lbs

3. Terminology

3.1 *Definitions of Terms Specific to This Standard:*

3.1.1 *barrier requirements, n*—the need to promote or inhibit moisture, gas, or light, or a combination thereof, while maintaining necessary levels of sterility.

3.1.2 *durability requirements, n*—material properties relevant to the ability of the package to protect the product.

3.1.3 *integrity and seal requirements, n*—the ability of the package to prevent inadvertent escape of contents or entrance of outside substances while preserving intended opening for use features.

3.1.4 *package performance, n*—the ability of the packaging system, including the sterile barrier system and protective packaging, to withstand the hazards of handling, distribution, and storage.

3.1.5 *printing requirements, n*—the printed ink properties needed to ensure physical and chemical resistance to degradation.

3.1.6 *processing requirements, n*—the material characteristics needed to ensure the consistent and reliable production of the package.

3.1.7 *safety requirements, n*—safeguard product against contamination and deleterious health effects.

3.1.8 *visibility and appearance requirements, n*—the desired package aesthetics needed to permit or inhibit viewing of the product or to enhance product presentation.

3.2 For other terms used in this guide, see Terminology F17.

4. Significance and Use

4.1 This design and evaluation guide describes multiple categories for evaluating flexible medical packages and packaging materials. These include safety, barrier properties, durability, package and seal integrity, visibility and appearance, processing, printing ink properties, and package performance.

[4] Available from International Organization for Standardization (ISO), 1 rue de Varembé, Case postale 56, CH-1211, Geneva 20, Switzerland, http://www.iso.ch.
[5] Available from Standardization Documents Order Desk, Bldg. 4 Section D, 700 Robbins Ave., Philadelphia, PA 19111-5094, Attn: NPOPS.
[6] Available from Technical Association of the Pulp and Paper Industry (TAPPI), 15 Technology Parkway South, Norcross, GA 30092, http://www.tappi.org.
[7] Available from International Safe Transit Association (ISTA), 1400 Abbot Rd., Suite 160, East Lansing, MI 48823-1900, http://www.ista.org.

4.2 The intent of this design and evaluation guide is to evaluate all cited categories and select those that are applicable. Once the product has been characterized and the sterilization methodology has been defined, there are numerous sets of requirements for any specific package. This design and evaluation guide provides an avenue for assessing these requirements and choosing test methods for both evaluating the package design and monitoring package compliance.

NOTE 1—Many of the standards included in this guide are consensus standards that are recognized by the United States Food and Drug Administration (FDA). Selection and use of a U.S. FDA recognized consensus standard is voluntary and the sole responsibility of the user in determining its applicability. For further information, consult the U.S. FDA Medical Device Standards Program at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Standards/default.htm.

4.3 Product characterization shall include mass or weight, geometry (length and width, height, and shape) and product composition.

4.4 All categories must be considered for applicability.

4.5 The Summary of Test Methods for Medical Packaging Design and Evaluation (Fig. 1) provides a compact graphical presentation of the test methods referenced in this guide.

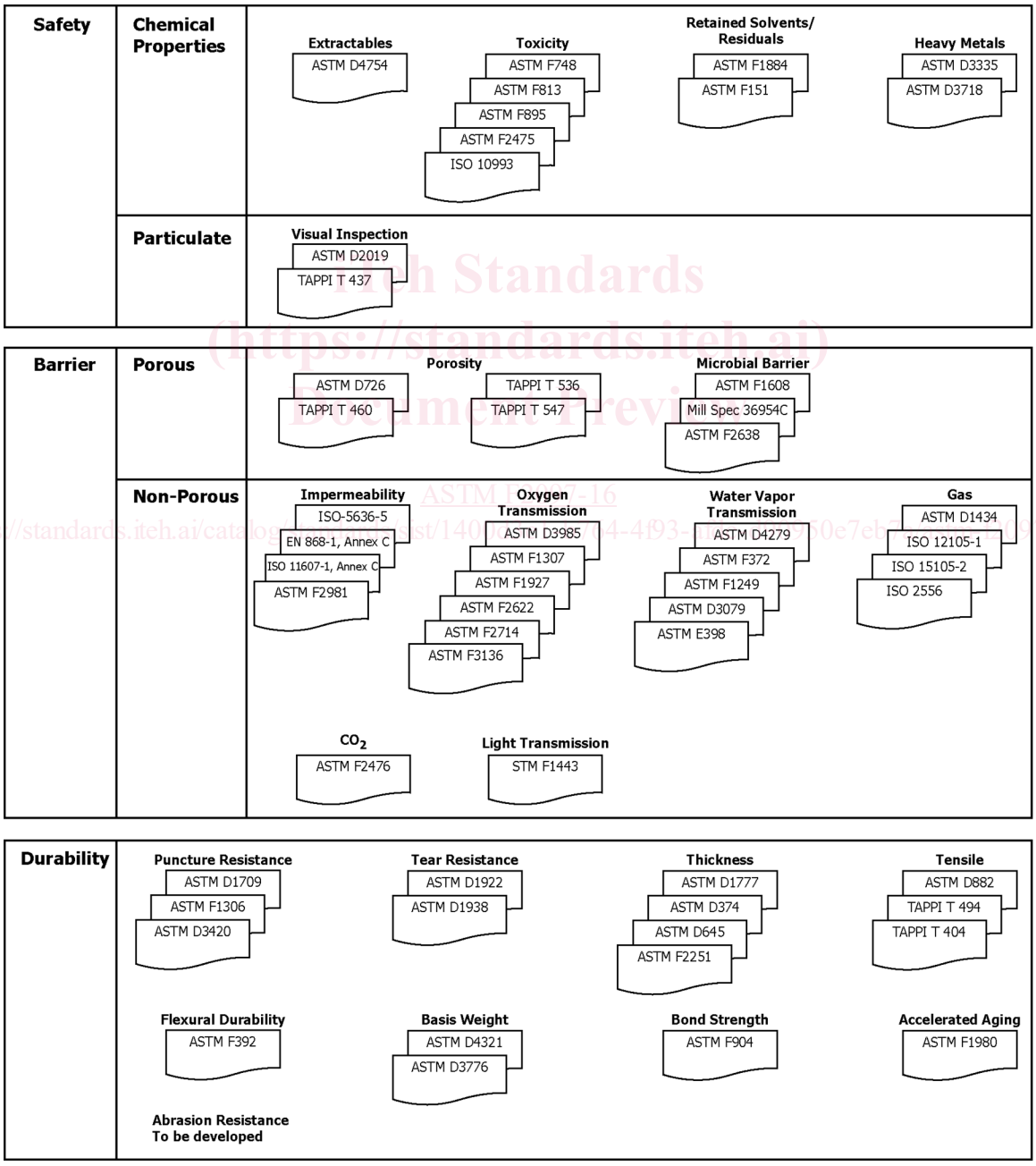

FIG. 1 Summary of Test Methods for Medical Packaging Design and Evaluation

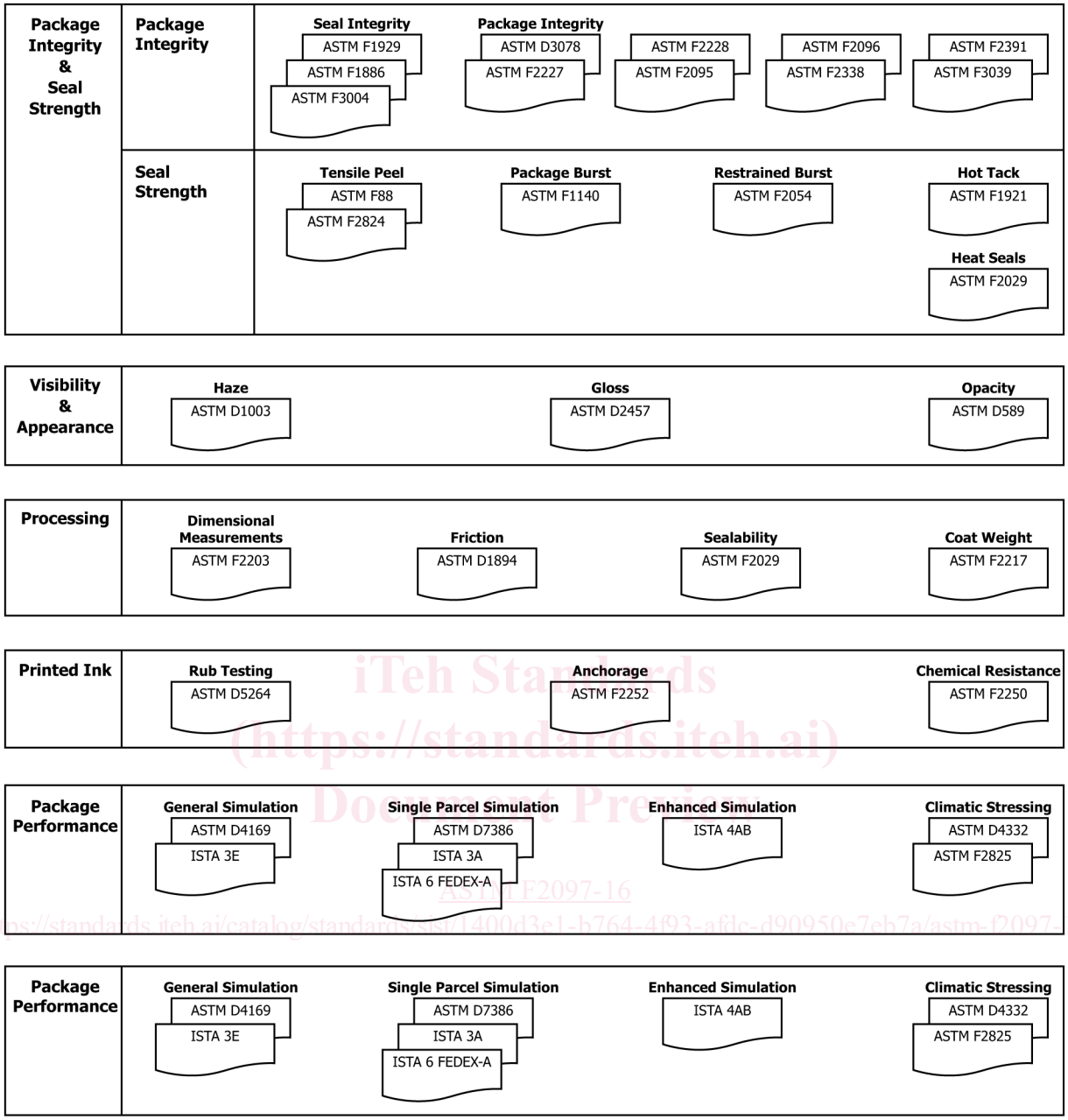

FIG. 1 Summary of Test Methods for Medical Packaging Design and Evaluation *(continued)*

4.6 *Test Description and Applicability* (see Table 1):

4.6.1 Table 1 lists the test methods commonly used to evaluate flexible medical packaging. The test methods are used in two phases.

4.6.1.1 *Package Design: Characterization of the Materials and Evaluation of the Resultant Package*—This is referred to as "R&D Evaluation" in Table 1. Testing during this phase is characterized by the generation of quantitative data on the performance of the component materials and the package assembly. These test methods are lengthy, making them inappropriate for the manufacturing environment where rapid response is required for process control. Often, they are expensive and require specialized equipment not readily available at a medical packaging or device manufacturing facility.

4.6.1.2 *Package Compliance: Routine Monitoring of Adherence to Specifications*—This is referred to as "Compliance Testing" in Table 1. Testing during this phase must be rapid, inexpensive, and readily implemented in a manufacturing environment. The objective is not to develop design data, but to ensure that the design specifications are being met. These test methods do not necessarily make direct measurements of critical values, but detect variations in material, process, or product that are indicative of all critical characteristics.

TABLE 1 Test Description and Applicability Table

Test	Test Method	Description	Applicability
		Safety Requirements	
		Chemical Properties	
Extractibles Usage R&D evaluation	ASTM D4754	This test method covers the use of the FDA migration cell in the extraction of components and permits quantitation of individual migrants from plastic materials by suitable extracting liquids, including liquid foods and food-stimulating solvents. This test method provides a two-sided, liquid extraction test for plastic materials that can be formed into film, sheet, or disks.	This test method has been applied to a variety of migrant/polymer systems in contact with numerous foods and food simulants. Though most of the migrants examined were radiolabeled, the use of the FDA cell has been validated for migration studies of unlabeled styrene from polystyrene. This test method has been shown to yield reproducible results under the conditions for migration tests requested by the FDA. However, if the data is to be submitted to the FDA, it is suggested that their guidelines by consulted. Because it employs two-sided extraction, this test method may not be suitable for multilayered plastics intended for single-sided food contact use. The size of the FDA migration cell as described may preclude its use in determining total nonvolatile extractives in some cases.
Toxity Usage R&D evaluation	ASTM F748	This practice recommends generic biological test methods for materials and devices according to end-use applications. Tests include those performed on materials, end products, and extracts. Rationale and comments on current state of the art are included for all test procedures described. Biological evaluation of materials and devices, and related subjects such as pyrogen testing and batch testing of production lots are also discussed.	The biocompatibility of materials used in single-component or multicomponent medical devices for human use depends to a large degree on the particular nature of the end-use application. It is not possible to specify a set of biocompatibility test methods which will be necessary and sufficient to establish biocompatibility for all materials and applications. While chemical testing for extractable additives and residual monomers or residues from processing aids is necessary for most implant materials, such testing is not included as a part of this practice. The reader is cautioned that the area of materials biocompatibility testing is a rapidly evolving field, and improved methods are evolving rapidly, so this practice is by necessity only a guideline. These test protocols are intended to apply to materials and medical devices for human application.
Toxity Usage R&D evaluation	ASTM F813	This practice describes a reference method of direct contact cell culture testing that may be used in evaluating the cytotoxic potential of materials for use in the construction of medical materials and devices. This practice may be used either directly to evaluate materials or as a reference against which other cytotoxicity test methods may be compared.	This practice tends to be used less frequently due to the risk of inducing a response from mechanical damage due to direct placement of the sample onto the cell layer. This practice may be suitable for products which have leachates that are not able to diffuse through agar and are not too heavy.
Toxicity Usage R&D evaluation	ASTM F895	The agar diffusion assay is an indirect contact test in which the test material is placed onto an agar layer that protects the cells. This test method is commonly used to evaluate the response of small samples that have at least one flat surface such as elastomeric closures.	This is one of a series of reference test methods for the assessment of cytotoxic potential, employing different techniques. Assessment of cytotoxicity is one of several tests employed in determining the biological response to a material, as recommended in Practice F748. This test method is appropriate for materials in a variety of shapes and for materials that are not necessarily sterile. This test method would be appropriate in situations where the amount of material is limited. For example, small devices or powders could be placed on the agar and the presence of a zone of inhibition of cell growth could be examined. While the agar layer can act as a cushion to protect the cells from the specimen, there may be materials which are sufficiently heavy to compress the agar and prevent diffusion or to cause mechanical damage to the cells. This test method is not appropriate for leachables that are not water soluble because they may not diffuse through agar or agarose and thus not be detected. This test method would not be appropriate for these materials. The L 929 cell line was chosen because it has a significant history of use in assays of this type. This is not intended to imply that its use is preferred; only that the L 929 is an established cell line, well characterized and readily available, that has demonstrated reproducible results in several laboratories.
Toxicity Usage R&D evaluation	ASTM F2475	This guide provides information to determine the appropriate testing for biocompatibility of packaging materials used to contain a medical device.	This method applies to packaging for medical devices.