
This standard is issued under the fixed designation F2743; 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 describes recommended in vitro test procedures for coating inspection and acute particulate characterization of coated drug-eluting vascular (balloon-expandable and self-expanding) stent systems.

1.2 Recommended practices for coating inspection and acute particulate characterization include baseline (deployment) testing and simulated use testing. This guide describes the capture and analysis of particulates. This guide describes the inspection of the coated stent surface. This guide was developed for characterization and not intended for production release testing of coated drug-eluting vascular stent systems although some sections may be appropriate.

1.3 Chronic particulate characterization and coating inspection are not included herein.

1.4 Coating systems specifically designed to degrade or otherwise intentionally separate themselves from the permanent stent structure may not be fully addressed herein.

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 The values stated in inch-pound units are to be regarded as standard. The values given in parentheses are mathematical conversions to SI units that are provided for information only and are not considered standard.

2. Referenced Documents

2.1 Other Standards:

USP <788> Particulate Matter in Injections
FDA Guidance for Industry and FDA Staff Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems, April 18, 2010
AAMI TIR42:2010 Evaluation of Particulates Associated with Vascular Medical Devices

3. Terminology

3.1 Definitions:

3.1.1 mock vessel—physical simulation of the vasculature at the intended clinical deployment site.

3.1.2 stent system—a system comprised of a vascular stent and its delivery system.

3.1.3 tracking—navigation of a guide wire, guide catheter, and/or stent system through either actual or simulated vascular anatomy.

3.1.4 tracking fixture—a model that simulates or replicates the geometry of a representative vasculature through which the stent system will be passed.

3.2 Definitions of Terms Specific to This Standard:

3.2.1 acute—a test timeframe intended to include stent delivery and deployment beginning with the initial insertion of stent system until full removal of the delivery system and its accessory devices.

3.2.2 baseline—coating inspection and acute particulate characterization after stent expansion to the desired diameter in an unconstrained environment and without tracking.

3.2.3 chronic—a test timeframe intended to mimic the implantation time after full removal of the delivery system and its accessory devices.

3.2.4 constrained environment—a deployment site in which the stent is deployed into a mock vessel.

3.2.5 simulated use—coating inspection and acute particulate characterization after tracking in simulated anatomy and aqueous environment. It may also include deployment in bent configuration, deployment in overlapped configuration, post-dilatation, or other scenarios that can reasonably be expected in clinical use.

3.2.6 unconstrained environment—a deployment site in which the stent is not constrained by a mock vessel. Compare to “Constrained Environment”.

4. Summary of Practice

4.1 Test Sequence and Samples—Baseline and Simulated Use Testing are conducted as two separate tests. Coating
inspection and acute particulate characterization may be performed as two separate tests with independent samples.

4.2 Baseline Testing—A single stent is deployed to nominal or maximum labeled diameter. The stent is expanded in an unconstrained environment so as to characterize the stent only. Baseline testing includes coating inspection and acute particulate characterization of the stent. Baseline coating inspection may be conducted after deployment in air or in an aqueous unconstrained environment. Baseline acute particulate characterization should be conducted in an aqueous unconstrained environment. The surfaces of the stent coating are inspected for defects or other adverse attributes caused by this procedure. Cumulative particulates released are captured or continuously monitored, counted and classified according to size ranges.

4.2.1 Particles released may be captured in a receptacle and sampled for count/size using light obscuration or filtration/microscopy, or

4.2.2 Particles released may be acquired and continuously counted in an apparatus (for example, tube) for facilitating flow.

4.3 Simulated Use Testing—The stent system is tracked in an aqueous environment, through an appropriately clean, in vitro model simulating the vascular anatomy to be navigated to access the targeted clinical deployment site. Accessory devices (for example, guidewires, guide catheters, and so forth) are utilized as indicated in the IFU. The stent is deployed either singly or overlapped with another stent and bent configuration to represent worst-case clinical condition, as appropriate. A constrained environment should be used as the deployment location. Stents should be expanded in accordance with the IFU, including expansion to post-dilatation limits, as appropriate. Cumulative particulates released from the stent(s), stent coating(s), stent system(s) and accessory devices (if used) during the procedure are captured or continuously monitored, counted and classified according to size ranges. Particulate characterization may be necessary to aid in classifying potential particulate sources, and the test developer should understand the constituents of the coated stent system. The surfaces of the stent coating(s) are inspected for defects or other adverse attributes caused by this procedure. Analysis of particulates and surface inspection may be accomplished using the same test articles subjected to tracking and deployment, if appropriate.

4.3.1 Particles released may be captured in a collection beaker and sampled for count/size using light obscuration or filtration/microscopy. The need for post-dilatation, overlapping or to limit self-expansion may require deployment into a mock vessel, or

4.3.2 Particles released may be captured in a collection beaker and sampled for count/size using light obscuration or filtration/microscopy. The need for post-dilatation, overlapping or to limit self-expansion may require deployment into a mock vessel, or

5. Significance and Use

5.1 The shedding of the coating from a vascular stent can alter its clinical safety and/or therapeutic benefit. Clinical performance (for example, drug elution) may be affected by particulate generation from the coated stent system and coating defects. This document provides guidance for coating inspection and acute particulate characterization of drug eluting vascular stents. Information about the potential for shedding can be gained during bench testing. The general guidelines presented here may be used for writing detailed protocols for specific products at the various stages of the product development process. Such testing may be performed during device development, design validation testing, lot-release testing, and/or stability testing although different requirements may apply at each stage. These suggested methods may represent a reasonable simulation of clinical usage. When establishing the coating inspection and acute particulate characterization testing conditions, the current clinical usage/practice (for example, post-dilation, overlapping stents) and the instructions for use (IFU), as applicable, should be considered. While methods for chronic particulate characterization and coating inspection have not been established, these suggested methods may be helpful in the development of chronic methods. Testing in accordance with recommendations in this guide will generate data that may lead to further improvements in the method and its validation, as well as possible advancements in device design and performance. See also FDA Guidance for Industry and FDA Staff and AAMI TIR42:2010.

6. Suggested Materials and Reagents

6.1 Baseline Testing:

6.1.1 Beaker.

6.1.2 Filtered (for example, 1.2 µm or finer), de-ionized or distilled water, in general accordance with USP <788>. Other solutions may be used if justified.

6.1.3 Heating system, capable of maintaining fluid temperature at 37 ± 2°C.

6.1.4 Particulate filter, 1.2 µm or finer, with appropriate holder

6.1.5 Particulate analyzer, capable of detecting and counting particulates in appropriate size ranges (for example, ≥10 µm).

6.1.6 Calibration standards for particulate sizing and counting.

6.1.7 Analytical instrumentation for particulate characterization [for example FTIR (Fourier transform infrared) spectroscopy, Raman Spectroscopy, Scanning Electron Microscope (SEM) with Energy Dispersive Spectroscopy (EDAX), X-ray photoelectron spectroscopy (XPS) or Time-of-flight secondary ionization mass spectroscopy (TOF-SIMS)] (if utilized).

6.1.8 Continuous flow particulate counting system (if utilized):

6.1.8.1 Apparatus (for example, tube) for facilitating flow and housing the test article in an unconstrained environment.

6.1.8.2 Pump for controlling fluid flow.

6.1.8.3 Continuous flow particulate counter.

6.2 Simulated Use:

6.2.1 Filtered (for example, 1.2 µm or finer), de-ionized or distilled water, in general accordance with USP <788>. Other solutions may be used if justified.

6.2.2 Tracking fixture, (see 3.1 and 7.3).

6.2.3 Heating system, capable of maintaining fluid temperature at 37 ± 2°C.

6.2.4 Mock vessel, (see 3.1 and 7.4).

6.2.5 Continuous flow particulate counting system:
6.2.5.1 Apparatus (for example, tube) for facilitating flow and housing the test article in a constrained environment.
6.2.5.2 Pump for controlling fluid flow.
6.2.5.3 Continuous flow particulate counter.
6.2.6 Collection Beaker, (optional).
6.2.7 Particulate filter 1.2 µm or finer, with appropriate holder (if utilized).
6.2.8 Particulate analyzer, capable of detecting and counting particulates in appropriate size ranges (for example, ≥10 µm).
6.2.9 Calibration standards for particulate sizing and counting.
6.2.10 Accessory devices per IFU (for example, guide catheter, guidewire, post-dilatation balloon catheter, and so forth).
6.2.11 Analytical instrumentation for particulate characterization [for example FTIR (Fourier transform infrared) spectroscopy, Raman Spectroscopy, Scanning Electron Microscope (SEM) with Energy Dispersive Spectroscopy (EDAX), X-ray photoelectron spectroscopy (XPS) or Time-of-flight secondary ionization mass spectroscopy (TOF-SIMS)] (if utilized).
6.2.12 Stent Surface Inspection—For complete characterization, inspection of the surface of the stent may be performed at different time points (for example, before expansion, after expansion to the nominal or maximum labeled diameter, and after simulated use). Representative photos should be provided for each step and region, as described further in Section 8. The location of the photographed regions should be predetermined. A lower magnification photograph(s) of the stent that includes and identifies the pre-specified locations should also be provided. The “before expansion” inspection of the stent may be performed prior to or after the stent is mounted on a delivery system; however, stent surface inspections made prior to stent system assembly (for example, crimping/loading) can make identifying the source of damage (for example, crimping/loading or tracking and deployment) difficult. Handling during the initial inspection may introduce particulates and contamination. Inspection of the stent mounted on/in the delivery system may be useful for assessing initial manufacturing quality and/or for establishing a baseline for determining when during the subsequent tracking/deployment process coating damage or particulate shedding may be occurring. Individual defects may be assessed throughout usage, if appropriate (for example, for investigative purposes). A stent may be inspected on all surfaces prior to loading onto the delivery system. Self-expanding stents are usually covered by an opaque sheath and may not be amenable to inspection after loading onto the delivery system.
6.2.13 After baseline expansion to nominal or maximum diameter.
6.2.14 After simulated use.
6.2.15 Inspections of stent surfaces may be performed by optical (light) microscopy, scanning electron microscopy (SEM), fluorescence microscopy, Raman spectroscopy, and so forth. Each technique offers advantages and disadvantages:
6.2.16 Optical (Light) Microscopy—See Table 1.
6.2.17 Scanning Electron Microscopy—See Table 2.
6.2.18 Fluorescence Microscopy—See Table 3.
6.2.19 Raman Spectroscopy—See Table 4.

### TABLE 1 Advantages and Disadvantages of Optical (Light) Microscopy

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>A. Lower magnification (typically &lt;200x) speeds coarse inspection</td>
<td>A. Limited resolution</td>
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<tr>
<td>B. May allow inspection of stent system</td>
<td>B. Smaller depth of field (focus depth) as compared to SEM</td>
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<td>C. No stent size limitations</td>
<td>C. Light reflections may mask features</td>
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<tr>
<td>D. Non-destructive</td>
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<tr>
<td>E. Color differentiation (if applicable)</td>
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