Designation: F2743 – 11

Standard Guide for
Coating Inspection and Acute Particulate Characterization of Coated Drug-Eluting Vascular Stent Systems[1]

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[2]

FDA Guidance for Industry and FDA Staff Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems, April 18, 2010[3]

AAMI TIR42:2010 Evaluation of Particulates Associated with Vascular Medical Devices[4]

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.

---

[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 F04.30 on Cardiovascular Standards.

Current edition approved Oct. 1, 2011. Published November 2011. DOI: 10.1520/F2743-11.

[2] Available from U.S. Pharmacopeia (USP), 12601 Twinbrook Pkwy., Rockville, MD 20852-1790, http://www.usp.org.

[3] Available from Food and Drug Administration (FDA), 10903 New Hampshire Ave., Silver Spring, MD 20993-0002, http://www.fda.gov.

[4] Available from Association for the Advancement of Medical Instrumentation (AAMI), 4301 North Fairfax Dr., Suite 301, Arlington, VA 22203-1633.

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 acquired and continuously counted in an apparatus (for example, tube) for facilitating flow.

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).

6.3 *Coating Inspection (Baseline and Simulated Use),* Optical microscope with appropriate lighting and camera and/or SEM.

6.4 *Test Articles*—Unless otherwise justified, all samples selected for testing should be clinical or commercial quality products (for example, complete stent systems). Environmental conditions (for example, aging, shipping, storage, and so forth) may affect the stent system and should be considered when assessing coating inspection and acute particulate characterization. Post-coating activities (for example, crimping, sterilization, balloon expansion) are critical for coating inspection and acute particulate characterization. A sufficient number of specimens should be tested to support any claims to be made based on the test results.

7. Test Method Considerations

7.1 *Environment*—It is extremely important that all procedures be performed in a controlled environment (that is, one which will not affect the integrity of the study). The meaningful characterization of size and quantity of small particulates shed by the coated stent can be significantly impacted by environmental contamination. Likewise, contamination on the stent surface may be misinterpreted as coating defects or may mask actual defects. Poor experimental technique and handling of accessory devices may also be significant sources of non coating particulates. Physical and chemical contamination, in addition to particulates, may impact the results of this characterization.

7.2 *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.

7.2.1 Summary of inspection steps which may be performed:

7.2.1.1 Before stent loading (if applicable).

7.2.1.2 Before expansion.

7.2.1.3 After baseline expansion to nominal or maximum diameter.

7.2.1.4 After simulated use.

7.2.2 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:

7.2.2.1 *Optical (Light) Microscopy*—See Table 1.

7.2.2.2 *Scanning Electron Microscopy*—See Table 2.

7.2.2.3 *Fluorescence Microscopy*—See Table 3.

7.2.2.4 *Raman Spectroscopy*—See Table 4.

7.2.3 Examples of commonly observed surface anomalies and defects are shown in Appendix X1. See also AAMI TIR42:2010.

7.3 *Simulated Use Tracking*—Tracking during simulated use should be through a model tortuous path that simulates the geometry of a typical severe anatomic path through which the stent system will be passed during clinical use. The tracking fixture should include both the portion of anatomy in which the stent system would be passed through the guide catheter and the portion through which it would be passed after exit from the guide catheter, if applicable. The appropriate geometry may be different for different intended deployment sites (for example, coronary, carotid, or femoral arteries) or for different access points (for example, femoral or radial artery). Critical features to be considered in selecting the appropriate tracking fixture include lumen diameter, bend radii, bend reversals,

TABLE 1 Advantages and Disadvantages of Optical (Light) Microscopy

Advantages	Disadvantages
A. Lower magnification (typically <200×) speeds coarse inspection	A. Limited resolution
B. May allow inspection of stent system	B. Smaller depth of field (focus depth) as compared to SEM
C. No stent size limitations	C. Light reflections may mask features
D. Non-destructive	
E. Color differentiation (if applicable)	

TABLE 2 Advantages and Disadvantages of Scanning Electron Microscopy

Advantages	Disadvantages
A. Greater depth of field (focus depth) compared to Optical Microscopy	A. May be a destructive test
B. Higher magnification (up to 10 000× magnification) enhances view of small features	B. May require sputter coating (except for environmental SEM), precluding the use of a single test article for multi-time point inspections
	C. Slower manipulation compared to Optical Microscopy
	D. Inspection of the full length stent may not be possible within the chamber
	E. Grey scale only

TABLE 3 Advantages and Disadvantages of Fluorescence Microscopy

Advantages	Disadvantages
A. Signal-to-noise ratio can help discern different types of product in mixture	A. High cost of capital equipment (that is, fluorescence microscope)
B. Non-destructive	B. Not many materials have intrinsic fluorescence

TABLE 4 Advantages and Disadvantages of Raman Spectroscopy

Advantages	Disadvantages
A. Can obtain spectroscopic data using aqueous solutions	A. High cost of capital equipment (that is, Raman spectrometer or attachment)
B. Non-destructive	B. Requires high sample concentration
C. Provides both chemical and structural information	

ability to clean and coefficient of friction of the tracking material (for example, polyurethane, silicone, Teflon, glass, latex or native vessel). The tracking lumen for the guide catheter path may be constructed of glass or other durable materials which minimize background noise particulate counts. If justifiable, surrogate ancillary devices (for example, mandrel for guidewire) may be used to aid in minimizing background noise.

7.4 *Simulated Use Deployment*—A single stent or two overlapped stents may be deployed and over expanded (if appropriate). Simulated use deployment should be into a mock vessel. If used the mock vessel should reasonably represent the intended clinical deployment site. Critical features to be considered in selecting the appropriate mock vessel include geometry (for example, inside diameter, length), mechanical properties, ability to remove stent without coating damage, coefficient of friction of the material (for example, polyurethane, silicone, latex and native vessel). Any particulates from the mock vessel will contribute to the total cumulative count unless their composition is characterized in order to exclude them from the total count but should be included in the test report. Means for extracting the deployed stent from the mock vessel without imposing additional damage to the coating will be necessary for the post-deployment inspection.

7.5 *Particulate Capture and Characterization:*

7.5.1 *Spiking and Recovery:*

7.5.1.1 An appropriate spiking and recovery study should be performed on each test system for baseline and simulated use. Spiking and recovery should be performed in the test system without the presence of a stent system.

7.5.1.2 Particulate standards representative of the sizes to be investigated should be used (for example, three particulate standards where at least one is greater than 50 µm). The number and size of particulates of the standard should be certified by the manufacturer or verified with a different method. Multiple injections at the location where the stent system would be introduced into the test fixture should be performed because this represents the worst case for particle capture efficiency. The same collection and counting techniques to be used during testing of the stent system should be used. Uniform distribution of particulates within the standard used for spiking as well as accurate volume for injection are critical to the success of the spiking and recovery study. The amount of particulates recovered during this test should meet a pre-specified level.

7.5.2 *Collection*—Particulate matter should be captured or continuously monitored and analyzed. For simulated use, particulates released from the stent system, beginning when the stent system is first inserted into the introducer or guide catheter and ending when the delivery and/or post-dilatation catheter is completely withdrawn, should be included. Since all particulates released during the acute phase of each type of evaluation can be considered as a single bolus, it may be collected and analyzed as a single sample. There may be advantages to collecting separate samples at different phases (for example, after tracking but before deployment, after each stent deployment if overlapping, after deployment but before post-dilatation, after post-dilatation).

7.5.3 *Chemical Characterization*—Chemical characterization of the particulate material may be necessary to differentiate coating and delivery system particulates from those from other sources (see 6.1.7 and 6.2.11). For example, if the stent is deployed into and subsequently extracted from a mock vessel, there may be silicone or latex particulates from that mock vessel mixed with stent coating and delivery system particulates or particulates introduced during the manufacturing process. It may be necessary to physically separate particulate material to facilitate chemical characterization.

7.5.4 *Sizing and Counting*—As suggested by USP<788>, the sizing and counting of particulates can be accomplished by light obscuration or by filtration and microscopic analysis. Each method has its advantages and disadvantages. Electrical zone counting (that is, Coulter principle) may also be used.

7.5.4.1 *Light Obscuration*—See Table 5.

7.5.4.2 *Filtration/Microscopy*—See Table 6.

8. Suggested Generic Test Methods

8.1 The following sections outline the suggested basic elements for Baseline testing (that is, no guide catheter, no tracking, and unconstrained deployment directly into air or an aqueous environment) and Simulated Use testing (that is, tracking and deployment in a constrained aqueous environment). Coating inspection and acute particulate characterization may be performed as separate tests, with independent samples, within Baseline and Simulated Use testing described below.

8.2 *Baseline Testing:*

8.2.1 *Initial Inspection*—Perform a coarse (for example, 25 to 50×) assessment of the as-manufactured stent coating and/or the accessible portion of the stent coating when the stent is mounted on the delivery system before deployment. Inspect all visible surfaces of the stent, noting and documenting the location of any coating anomalies, defects, or artifacts. For sheathed stents, inspect the stent prior to mounting onto the delivery system. Initial inspection may not be necessary if in-process inspection has been performed on the stent coating and coating defects, if any, have been documented. Examine any defects or other surface anomalies observed under coarse inspection under high magnification (for example, ~200×). If examination of defects or surface anomalies under high magnification jeopardizes the coating inspection (that is, adds particulate or damages the coating), it may be appropriate to utilize a separate set of samples that have not been through high magnification inspection for the particulate matter generation testing and the inspection after deployment in an unconstrained environment. Estimate the size and depth of defects by appropriate means (for example, image analysis software) and document their location. Document the condition of the overall coating by a sufficient number of representative images so that an assessment of coating consistency can be made.

8.2.2 *Blank/Background Assessment*—An appropriately clean system (that is, one that does not contain appreciable particulates) is desirable. Use cleaning procedures and test environment considerations in general accordance with USP<788>. Analyze the pre-deployment beaker or continuous flow solution to verify that it is sufficiently clean to allow an accurate assessment of coating particulates. Subtraction of blank/background particulates (that is, the amount of particulates in the beaker or continuous flow solution prior to deployment) is permitted with low counts and/or appropriate justification. Blank data should be recorded. It is up to the user to reduce background particulates since they will affect the reported total cumulative counts.

8.2.3 *Deployment*—Prepare the delivery catheter and deploy the stent to the desired diameter (for example, nominal, maximum labeled diameter), per the IFU. Testing can be conducted in either an aqueous system or air for coating inspection, but should be conducted in an aqueous environment for particulate characterization. The test system should be

TABLE 5 Advantages and Disadvantages of Light Obscuration

Advantages	Disadvantages
A. Fast	A. Incapable of characterizing particulate composition
B. Ability to select particulate size windows for automatic sorting and counting	B. Artifacts from air bubbles and lubricants
C. Theoretically allows counting of 100 % of particulates	C. May miss particulates due to shadowing
	D. Calibration required (for example, standard spheres)
	E. High cost of capital equipment
	F. Inaccurate particulate sizing due to non-spherical particulates
	G. Limited maximum particle size

TABLE 6 Advantages and Disadvantages of Filtration/Microscopy

Advantages	Disadvantages
A. Ability to infer particulate source by color and/or appearance	A. Time consuming for exhaustive analysis, may require partial count procedure
B. Amenable with EDAX or Raman Spectroscopy for composition characterization	B. Sampling errors if using partial count procedure
C. Insensitive to bubbles and lubricants	C. Counting and sizing errors due to agglomeration
	D. Requires additional handling (for example, transfer from beaker to filter, filter to microscope)
	E. Validation of image analysis software may be required
	F. Poor repeatability and reproducibility of manual counts

thermally controlled at 37 ± 2°C using aqueous media (see Section 6). Similar control of air deployment temperature is recommended. For quantitative particulate measurement, deployment into an unconstrained environment is necessary. A method to constrain a self-expanding stent may be required to obtain a clinically relevant deployment. For coating inspection only, deployment into air is permissible. If deployment is conducted in air for inspection only, particulate measurement does not apply; however, additional test article(s) would be required for particulate testing. Perform post-dilatation of the stent as appropriate. Remove the delivery and/or post-dilatation system(s).

8.2.4 *Rinse/Flush*—Agitate or flush the deployed stent with enough water to rinse released particulates in an unconstrained environment. Verify that particulates have been captured from the system using the results of spiking and recovery experiments (see 7.5.1) or by monitoring particle counts using sequential flushes. Care should be taken not to damage the coating when removing particulates.

8.2.5 *Post Deployment Inspection*—Remove the stent from the beaker or unconstrained environment and allow it to air dry in a controlled environment. Perform a coarse inspection (for example, 25 to 50×) of the stent, both outer and inner surfaces, noting and documenting any coating anomalies and defects. Perform a high-magnification (for example, ~200× or higher) inspection of any areas containing surface defects or anomalies. Re-examine the locations of any defects or anomalies found during the initial inspection, if applicable. Also examine under high magnification a representative sampling of the high-strain areas of the as-deployed or as–loaded stent as predicted by pre-specified analysis. Estimate the sizes of defects by appropriate means (for example, image analysis software or manually). Document the condition of the overall coating by a sufficient number of representative images so that an assessment of coating consistency can be made.

8.2.6 *Particulate Characterization*—Transfer the contents of the beaker for particulate analysis (for example, onto the filter for microscopic analysis or into the optical particulate analyzer). Verify complete transfer of all particulates from the beaker, if utilized, using repeated rinsing or other means. Perform a chemical characterization of the particulates unless appropriately justified (for example, technical limitations, low levels).

8.2.7 *Data Collection*—Determine the total cumulative number of particulates released from the stent using procedures in general accordance with the particulate characterization methods outlined in USP<788>. Determine the number of particulates in appropriate size ranges (for example, ≥10 µm, ≥25 µm, ≥50 µm) or bins (for example, 10 µm ≤ x ≤25 µm). Evaluate additional size ranges and particulate sizes if desired.

8.3 *Simulated Use Testing:*

8.3.1 *Initial Inspection*—Perform a coarse (for example, 25 to 50×) assessment of the as-manufactured stent coating and/or the accessible portion of the stent coating when the stent is mounted on the delivery system before tracking and deployment. Inspect all visible surfaces of the stent, noting and documenting the location of any coating anomalies, defects or artifacts. For sheathed stents, inspect the stent prior to mounting on the delivery system. Initial inspection may not be necessary if an in-process inspection has been performed on the stent coating and coating defects, if any, have been documented. Examine any defects or other surface anomalies observed under coarse inspection under high (for example, ~200×) magnification. If examination of defects or surface anomalies under high magnification jeopardizes the coating inspection (that is, adds particulates or damages the coating), it may be appropriate to utilize a separate set of samples that have not been through high magnification inspection for the particulate matter generation testing and the inspection after simulated use. Estimate the sizes and depth of defects by appropriate means (for example, image analysis software) and document their locations. Document the condition of the overall coating by a sufficient number of representative images so that an assessment of coating consistency can be made.

8.3.2 *Pre-flush*—Pre-flush the tracking fixture, guide catheter, guide wire, accessories and continuous flow apparatus (if utilized) with purified water, capturing any particulates released.

8.3.3 *Blank/Background Assessment*—Assess the pre-flush particulate counts. An appropriately clean system (that is, one that does not generate appreciable particulates from continued flushing) is desirable. Use cleaning procedures and test environment considerations in general accordance with USP<788>. Analyze the released solution and verify that the blank is sufficiently clean to allow an accurate assessment of coating particulates. Blank/background particulate subtraction is permitted with low counts and/or appropriate justification. Blank data should be recorded. It is up to the user to reduce background particulates since they will affect the reported total cumulative counts.

8.3.4 *Tracking*—Prepare the stent system and all accessories and track through the appropriate tracking fixture, in accordance with the IFU. Repeat the procedure using a number of tracking steps appropriate for the clinical indication and/or IFU. Use accessory devices (for example, introducer, guidewire, guide catheter, and so forth) as appropriate. The entire portion of the stent system that is intended to enter the body and tracking fixture should be tracked in aqueous environment maintained at 37 ± 2°C (see Section 6) unless otherwise justified.

8.3.5 *Deployment*—Deploy the stent or overlapped stents according to the IFU. If applicable (for example, balloon expandable stent), deploy using rated burst pressure. A constrained environment should be used. The mock vessel may be submersed in aqueous media (see Section 6) or be part of a continuous aqueous flow loop. The mock vessel may be in a clinically relevant bent configuration. The stent should be apposed to the mock vessel wall after expansion without the use of lubricants or other aides. Use post-dilatation, if appropriate. Completely withdraw the delivery and/or post-dilatation catheter.

8.3.6 *Rinse/Flush*—Flush the guide catheter, tracking fixture and stented mock vessel with enough water to capture released particulates. Flushing of the stented mock vessel or the tracking fixture might not be required if continuous flow is used. Verify that particulates have been captured from the system using the results of spiking and recovery experiments (see 7.5.1) or by monitoring particle counts using sequential flushes. Care should be taken not to damage the coating when flushing the system.

8.3.7 *Removal*—Remove the stent from the mock vessel (if used). Care should be taken not to damage the stent coating.

8.3.8 *Post Usage Inspection*—Perform a coarse (for example, 25 to 50×) inspection of the stent, on all surfaces, noting and documenting any coating anomalies, defects or artifacts. Perform a high (for example, ~200× or higher) magnification inspection of any areas containing surface defects or surface anomalies. Re-examine the locations of any defects or anomalies found during the initial inspection, if applicable. Also examine under high magnification a representative sampling of the high-strain areas of the as-deployed or as–loaded stent as predicted by analysis. Estimate the sizes of defects by appropriate means (for example, image analysis software or manually). Document the condition of the overall coating by a sufficient number of representative images so that an assessment of coating consistency can be made.

8.3.9 *Particulate Characterization*—Transfer the contents to the collection beaker for particulate analysis (for example, onto a filter for microscopic analysis or into the optical particulate analyzer). Verify, using repeated rinsing or other means, complete transfer of particulates from the collection beaker. Continuous particulate counting eliminates the need to transfer and sample. Perform a chemical characterization of the particulates unless appropriately justified (for example, technical limitations, low levels).

8.3.10 *Data Collection*—Determine the total cumulative number of particulates released from the stent system using procedures in general accordance with the particulate characterization methods outlined in USP<788>. Determine the number of particulates in appropriate size ranges (for example, ≥10 µm, ≥25 µm, ≥50 µm) or bins (for example, 10 µm ≤ x ≤25 µm). Evaluate additional size ranges and particulate sizes if desired.

9. Report

9.1 The test report should include a complete summary of the materials, methods and results, including any rationale for any deviations from the generic test method provided herein. The effects of any such deviations on the significance of the test results should be reported. All artifacts and anomalous observations should be reported, including justification for considering negative findings as artifacts or discounting their clinical significance.

9.2 *Example Test Report:*

9.2.1 Test Method and Acceptance Criteria, including scientific rationale for all chosen test parameters and criteria.

9.2.2 *Test specimen information:*

9.2.2.1 Traceability information (for example, number of test specimens, number of batches from which stents were selected).

9.2.2.2 Size (for example, diameter, length, or other relevant dimensions) of all test specimens.

9.2.2.3 Rationale for the number of test specimens, sizes used and the deployed stent configurations.

9.2.2.4 Rationale for use of any specimens that are not finished, sterilized product.

9.2.2.5 Sterilization methods and number of sterilization cycles applied to the test specimens.

9.2.3 Equipment and materials used, including, at a minimum, a complete description and schematics of the tracking fixture and its clinical relevance, rationale for the model, test time, accessory devices, filters, microscopes, equipment used for chemical characterization and image analysis software.

9.2.4 Summary of spike and recovery data.

9.2.5 Protocol deviations.

9.2.6 Test results, including total cumulative number of particulates (including blank counts), particulate size, and chemical characterization (if applicable).

9.2.7 Written and representative photographic descriptions of surface anomalies per the protocol.

9.2.8 Data analysis.

9.2.9 Conclusions regarding conformance with acceptance criteria and suitability for clinical use.

10. Keywords

10.1 baseline; coating inspection; DES; drug-eluting vascular stent; particulate; particulate characterization; simulated use

APPENDIX

(Nonmandatory Information)

X1. SEM PHOTOGRAPHS OF ANOMALIES AND DEFECTS

X1.1 See Figs. X1.1-X1.6.

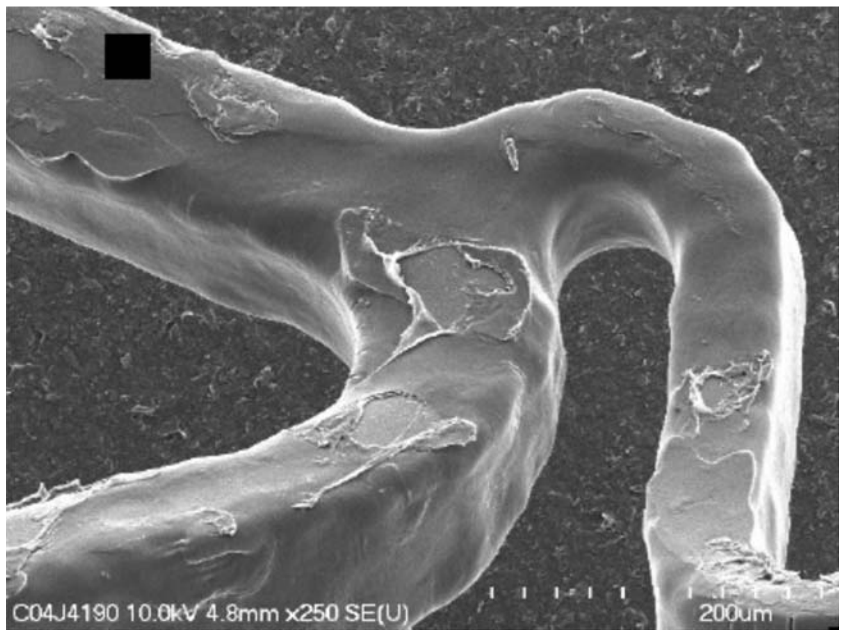

FIG. X1.1 Example of Flaking

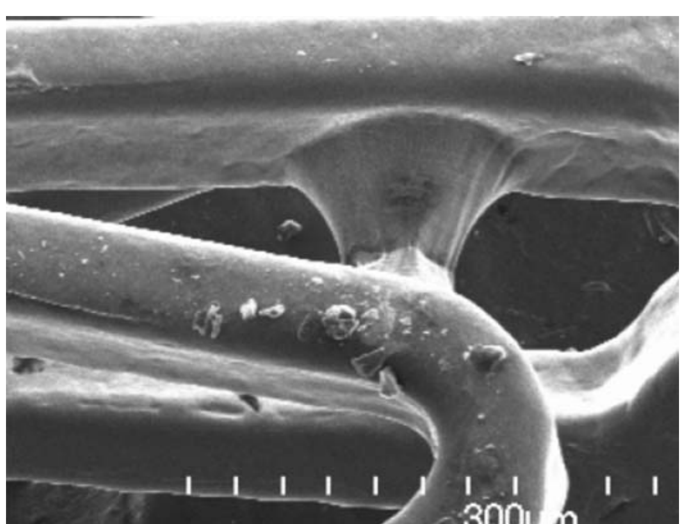

FIG. X1.2 Example of Webbing

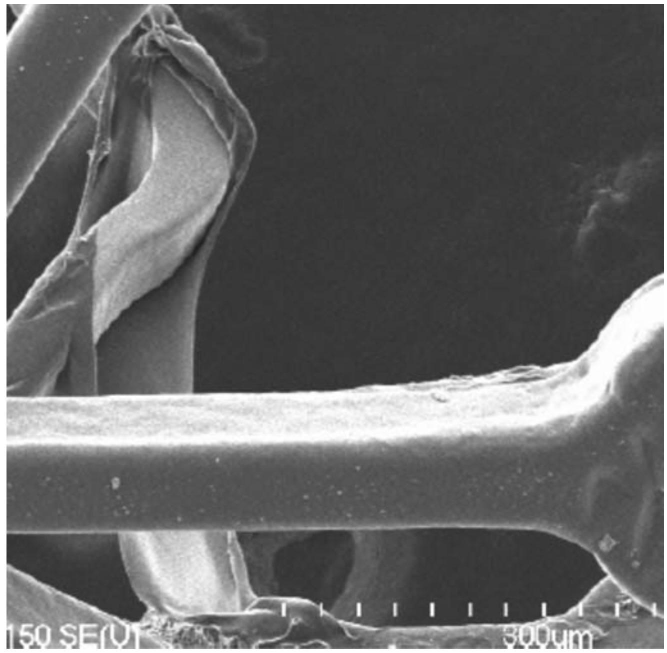

FIG. X1.3 Example of Delamination

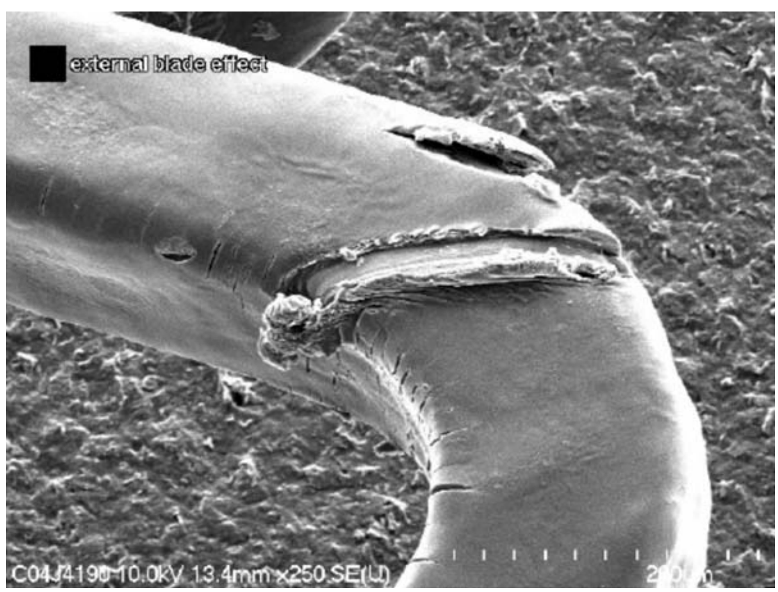

FIG. X1.4 Example of Artificial Cutting

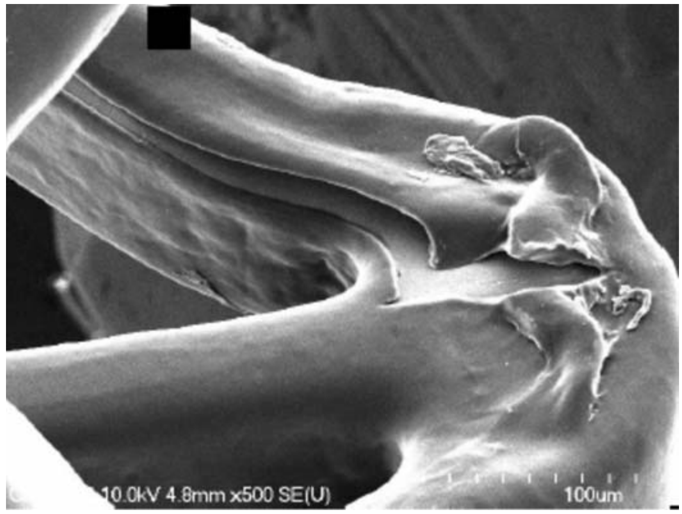

FIG. X1.5 Example of Delamination with Cutting

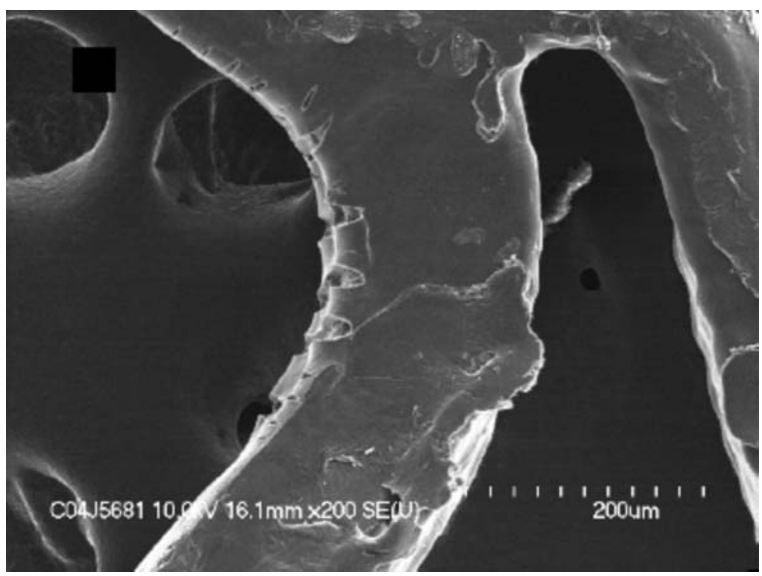

FIG. X1.6 Example of Imperfections