Class II Special Controls Guidance Document for Certain Percutaneous Transluminal Coronary Angioplasty (PTCA) Catheters

Document issued on: September 8, 2010
The draft of this document was issued May 30, 2008.

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Center for Devices and Radiological Health

Interventional Cardiology Devices Branch
Division of Cardiovascular Devices
Office of Device Evaluation

Preface

Public Comment

Written comments and suggestions may be submitted at any time for Agency consideration to the Division of Dockets Management, Divisions of Management Systems and Policy, Office of Human Resources and Management, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. Alternatively, electronic comments may be submitted to **http://www.regulations.gov (http://www.regulations.gov/)**. When submitting comments, please refer to docket number 2008D-0275. Comments may not be acted upon by the Agency until the document is next revised or updated.

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Guidance for Industry and FDA Staff Class II Special Controls Guidance Document for Certain Percutaneous Transluminal Coronary Angioplasty (PTCA) Catheters; Guidance for Industry and FDA

I. Introduction

This guidance document was developed as a special control to support the reclassification of certain Percutaneous Transluminal Coronary Angioplasty (PTCA) catheters into class II (special controls). The device is intended for balloon dilatation of a hemodynamically significant coronary artery or bypass graft stenosis in patients evidencing coronary ischemia for the purpose of improving myocardial perfusion; treatment of acute myocardial infarction; treatment of in-stent restenosis (ISR) and/or post-deployment stent expansion. This guidance does not apply to cutting/scoring PTCA catheters.

On December 4, 2000, the Circulatory System Devices Panel recommended that certain PTCA catheters be reclassified from class III to class II with special controls. This guidance is issued in conjunction with a *Federal Register* notice announcing the issuance of an order reclassifying this device type.

Following the effective date of an order reclassifying the device, any firm submitting a 510(k) for a PTCA catheter will need to address the issues covered in the special control guidance. However, the firm need only show that its device meets the provisions of the guidance or in some other way provides equivalent assurances of safety and effectiveness.

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II. Background

FDA believes that special controls, when combined with the general controls, will be sufficient to provide reasonable assurance of the safety and effectiveness of PTCA catheters, other than cutting/scoring PTCA catheters. Thus, a manufacturer who intends to market a device of this generic type must (1) conform to the general controls of the Federal Food, Drug, and Cosmetic Act (the act), including the premarket notification requirements described in 21 CFR 807, Subpart E, (2) address the specific risks to health associated with PTCA devices identified in this guidance, and (3) obtain a substantial equivalence determination from FDA prior to marketing the device.

This special controls guidance document identifies the classification regulation and product code for PTCA catheters (Please refer to **Section III. Scope)**. In addition, other sections of this special controls guidance list the risks to health identified by FDA and describe measures that, if followed by manufacturers and combined with the general controls, will generally address the risks associated with these PTCA catheters and lead to a timely 510(k) review and clearance. This document supplements other FDA documents regarding the specific content requirements of a premarket notification submission. You should also refer to 21 CFR 807.87, Format for Traditional and Abbreviated 510(k)s**[1]** and the section of CDRH's Device Advice, How to Prepare a 510(k) Submission. **[2]**

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III. Scope

The scope of this document is limited to percutaneous transluminal coronary angioplasty (PTCA) catheters as described below in 21 CFR 870.5100 (a). The product code associated with this device is LOX [percutaneous transluminal coronary angioplasty (PTCA) catheter].

Section 870.5100. Percutaneous Transluminal Coronary Angioplasty (PTCA) Catheter.

(a)*Standard PTCA catheter* –

(1) *Identification*. A PTCA catheter is a device that operates on the principle of hydraulic pressurization applied through an inflatable balloon attached to the distal end. A PTCA balloon catheter has a single or double lumen shaft. The catheter features a balloon of appropriate compliance for the clinical application, constructed from a polymer. The balloon is designed to uniformly expand to a specified diameter and length at a specific pressure as labeled, with well characterized rates of inflation and deflation and a defined burst pressure. The device generally features a type of radiographic marker to facilitate fluoroscopic visualization of the balloon during use. A PTCA catheter is intended for balloon dilatation of a hemodynamically significant coronary artery or bypass graft stenosis in patients evidencing coronary ischemia for the purpose of improving myocardial perfusion. A PTCA catheter may also be intended for the treatment of acute myocardial infarction; treatment of in-stent restenosis (ISR) and/or post-deployment stent expansion.

(2) *Classification*.Class II (special controls). The special control for this device is FDA's "Class II Special Controls Guidance Document: Percutaneous Transluminal Coronary Angioplasty (PTCA) Catheters." See §870.1(e) for the availability of this guidance document.

(b)*Cutting/scoring PTCA Catheter* –

(1) *Identification*. A cutting/scoring PTCA catheter is a balloon-tipped catheter with cutting/scoring elements attached, which is used in those circumstances where a high pressure balloon resistant lesion is encountered. A cutting/scoring PTCA catheter is intended for the treatment of hemodynamically significant coronary artery stenosis for the purpose of improving myocardial perfusion. A cutting/scoring PTCA catheter may also be indicated for use in complex type C lesions or for the treatment of in-stent restenosis.

(2)*Classification*. Class III (premarket approval). As of May 28, 1976, an approval under section 515 of the act is required before this device may be commercially distributed. See § 870.3.

Cutting/scoring PTCA catheters (procode NWX) remain in class III and continue to require premarket approval.

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IV. Device Description

We recommend that you identify your device by regulation and product code described in **Section III. Scope,** and include the following information:

Device components and theory of operation

We recommend that you identify all components and accessories included in the submission.

Photograph or drawing of the device

We recommend that you provide a photograph or drawing of the device, as well as a functional block diagram (including all accessories). If additional diagrams, dimensions, tolerances, and/or schematics are useful to fully describe and characterize the device, we recommend that you include them for each device, accessory or component included in the 510(k) submission.

Technological characteristics

We recommend that you describe the technical and performance specifications and include a brief description of the device design requirements in this section. The specifications may include performance-related product measurement tolerances, operating limitations, and any other functional, physical, and environmental specifications of the device. We also recommend that you describe ranges and/or accuracy of the specifications.

Patient-contacting materials

We also recommend that you provide a list of all patient contacting components and their respective materials. For each component, you should identify the generic material of construction and the unique material identifier.

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V. Risks to Health

In **Table 1** below, FDA has identified the risks to health generally associated with the use of the PTCA devices addressed in this document. The measures recommended to mitigate these identified risks are given in this guidance document, as shown in **Table 1** below. We recommend that you conduct a risk analysis to identify any other risks specific to your device and include the results of this analysis. If you elect to use an alternative approach to address a particular risk identified in this document, or have identified risks additional to those in this document, you should provide sufficient detail to support the approach you have used to address that risk.

Table 1: Risk / Mitigation Recommendations for PTCA Devices

Identified Risk	**Recommended Mitigation Measures**
Adverse Tissue Reaction	Section VI. Biocompatibility Testing
Device Failure	Section VIII. Performance Testing Section XI. Sterilization and Shelf Life
Adverse Interaction with Other Devices	Section VIII. Performance Testing Section IX. Animal Testing
User Error	Section IX. Animal Testing Section X. Clinical Information Section XII. Labeling
Vessel Damage	Section IX. Animal Testing Section X. Clinical Information
Infection	Section XI. Sterilization and Shelf Life

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VI. Biocompatibility Testing

FDA recommends that you conduct biocompatibility testing as described in the FDA guidance, **Use of International Standard ISO-10993, Biological Evaluation of Medical Devices Part-1: Evaluation and Testing**, for external devices in contact with the circulating blood for a limited duration (i.e., less than 24 hours).**[3]** We recommend that you select biocompatibility tests appropriate for the duration and level of contact with your device. If identical materials and identical material processing are used in a predicate device with the same type and duration of patient contact, you may identify the predicate device in lieu of providing biocompatibility testing.

Sample Preparation

It is important to understand how the test samples compare to the final sterilized product. For biocompatibility testing conducted using extraction samples, we recommend that you:

- determine the appropriate amount of test material as outlined in **ISO 10993-12** or an equivalent method, using surface area to extractant volume ratios (mass to extractant volume ratios should only be used if surface area cannot be calculated)
- use both polar and nonpolar extractants
- describe the condition of the extraction vehicle (e.g., color, presence of any particles)
- explain any changes in the post-extraction vehicle (compared to pre-extraction)
- describe the details of storage conditions, if applicable.

If extraction samples are not used immediately, we recommend that you follow the storage conditions described in **ISO 10993-12** or an equivalent method. We also recommend that you explain how storage does not affect your test results.

You should also consider the following additional recommendations when conducting your biocompatibility assessment:

Cytotoxicity

We recommend that extractions be conducted at 37°C for 24 hours using a vehicle with both mammalian cell culture media (MEM) and 5% serum, as these materials will allow for extraction of both polar and nonpolar constituents from the test sample.

Sensitization (Guinea Pig Maximization Method)

We recommend that test reports confirm that all female animals used in the testing are not pregnant, as pregnancy can reduce the ability of a female animal to detect a sensitization response.

We recommend either that you run concurrent controls, or that the test laboratory run controls within 3 months of the test samples. We also recommend you provide protocols and results from positive control testing to confirm that you used the same methods for both the positive control testing and the test samples.

Hemocompatibility

For blood-contacting devices (regardless of contact duration), we recommend that you consider hemolysis, immunology (complement activation), and *in vivo* thromboresistance.

Immunology testing should appropriately address the various complement activation pathways. We recommend that you assess *in vitro* C3a and SC5b-9 fragment activation using standard testing methods, such as those outlined in **ASTM F2065-00e1[4]** and **ASTM F1984-99 (2003)[5],** or an equivalent method. Alternatively, you may provide a rationale for omitting this testing, if all the materials used in the formulation and processing of the device have a history of previous use in blood-contacting devices with similar contact duration.

In addition, you may assess *in vivo* thrombogenicity during preclinical animal testing in lieu of a separate canine *in vivo* thrombogenicity test. If a 4 hour canine *in vivo* thrombogenicity study is needed (e.g., due to the use of novel materials never before used in a medical devices or questionable findings from the vascular animal studies), we recommend the study be conducted in a venous, unheparinized model.

Genotoxicity

Genotoxicity testing should be performed if new materials are included that have never been used in blood-contacting devices or implants in order to evaluate the genotoxic response to any particulates and leachables which still may be present after the catheter is removed from the body. **[6]**

Material-mediated Pyrogenicity

We recommend that you assess pyrogenic responses to chemical leachants over the duration of device contact with the patient. We recommend that you assess material-mediated pyrogenicity using traditional biocompatibility extraction methods, such as those outlined in the **USP 28 <151> Rabbit Pyrogen Test** (e.g., 50°C for 72 hours; 70°C for 24 hours; or 120°C for 2 hours) or an equivalent method. You should consider that temperatures above 37°C may result in toxicities not representative of the final product.

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VII. Content and Format of Test Data

A. Summary Reports

For traditional 510(k) submissions, we recommend that you present test data in a summary that includes the elements described below.

Table of Contents

You should place a table of contents at the front of the document. Each line listing in the table of contents should refer to major section titles and the page numbers where each section can be found.

Test Summaries

We recommend that you briefly describe all tests performed. If you follow an FDA- recognized standard without deviation, you may choose to reference that standard instead of describing the test methods.

Test Data Summaries

You should include test data summaries for all tests. The summaries should contain:

- minimum measured value (min)
- maximum measured value (max)
- mean
- standard deviation of the test data (std. dev.).

Summary of Conclusions

You should summarize your conclusions regarding whether the results support the safety and effectiveness of your device for each test.

You should include full test reports for all tests performed, as described below.

B. Test Reports

You should include full test reports for all tests performed. Your test reports should include the sections described below.

Test Specimen Information

Your test specimen description should include:

- number of test specimens
- size (diameter, length, or other relevant dimensions) of all test specimens

- rationale for the number of test specimens and sizes tested
- whether the specimens are representative of the finished product
- sterilization parameters and number of sterilization cycles applied to the test specimens.

Test Protocol

You should submit your test method or protocol. It should contain enough detail that an individual familiar with intravascular catheter testing will be able to interpret the test results. See Section C below.

Protocol Deviations

You should describe any protocol deviations and their impact on the conclusions you draw from the test.

Test Parameters and Acceptance Criteria

You should report the test parameters and acceptance criteria that you use, including:

- an explanation of and rationale for critical test parameters
- specifications or acceptance and rejection criteria
- a rationale for the specification or acceptance and rejection criteria based on the clinical requirements of the device.

Raw Data

We recommend that you include all raw data in appendices, or make the raw data available for our review upon request.

Test Results

You should summarize your test results and include statistical analysis when it is appropriate.

Data Analysis

You should analyze the data, including any outlying points and anomalous results, and explain whether the data meet the given acceptance criteria.

Conclusions

We recommend that you describe the conclusions drawn from the test results, and the clinical significance of the conclusions.

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C. Test Protocols

You should establish protocols for all experiments or computational analyses, including acceptance criteria when applicable, before you perform the tests. Established test protocols help to ensure consistent repetition of tests and allow comparison of data between test runs.

We recommend that you present test protocols to us before conducting tests. We will review your protocol and provide comments. Our input before testing may improve your ability to demonstrate the performance characteristics of your device.**[7]**

Your test protocols should assess device performance when exposed to the most extreme clinical conditions that your device is likely to experience. Both device configuration and physiologic conditions affect the performance of devices in the human body. We recommend that you evaluate extreme device dimensions, tolerances, sizes (e.g., maximum and minimum), and any other important device parameters in your testing program. We also recommend that you examine the outer limits of physiologic variables such as blood pressure, vascular compliance, and anatomic types. You should clearly state all test conditions in the test protocol and support them with references to applicable literature, standards, or both.

Occasionally, the worst performing combination of device configuration and physiologic conditions occurs in the mid-range of the relevant variables. You should check for this situation when developing your protocols to ensure that you test the worst performing combination.

The tests we describe in this guidance are those we generally have reviewed in PTCA catheter submissions and that we have considered necessary in the past to support the safety and effectiveness of these devices. Certain tests, however, may apply only to specific designs or clinical indications. These tests are identified under separate headings. We believe that each test helps to support the safety and effectiveness of PTCA catheters. Each test's clinical or engineering significance is described.

For PTCA catheters with certain indications, some of the tests in this guidance may not apply. If you believe a test recommended in this guidance does not apply to your device, you should include a heading for the test in your test summary, followed by an explanation of why the test is not applicable. We will then be aware that you did not inadvertently omit it from your application.

Your explanation should include a rationale for why you think the test is not applicable to your device. Your rationale should clearly demonstrate, by reference to a Failure Modes and Effects Analysis (FMEA) or other risk analysis method, that the particular test or data set is not applicable. Alternatively, you may identify measures you have taken to mitigate the risks associated with the device in the failure mode that would usually be evaluated using the test that you have not performed.

Sample Selection

You should use a statistically significant sample size whenever possible. When using a statistically significant number of samples is not possible, you should provide a scientific rationale to support the number of samples tested in your test summary and test protocols, and provide reasonable assurance that the test results support the safety and effectiveness of the device.

We recommend you conduct testing on the finished product. The devices you test should be sterilized by the final production process, including repeat sterilization cycles. If you conduct testing on any samples that are not finished, sterilized product, we recommend you indicate this in the test protocols and test summary, and explain why doing so does not affect the applicability of the test results to the evaluation of substantial equivalence.

You should test the full range of sizes that you intend to market. The recommended default paradigm is a 2 x 2 factorial of the largest and smallest diameters and lengths, also known as the "four corners" paradigm for each different device design. We recommend a different set of sizes for some of the tests in this section.

Table 2 illustrates the four corners concept for a typical PTCA catheter. If you do not test a device using the four corners paradigm or the recommended sizes for a particular test, you should provide a scientific rationale to support the sizes that you do test in the test summary and test protocols. For some tests, we may recommend that you perform an analysis to identify the size or sizes that represent the worst case.

Table 2: Four Corners Test Paradigm Example

Balloon Diameter (mm)	Balloon Length (mm)			
	10	20	30	40
2.0	X			X
2.25				
2.5				
2.75				
3.0				
3.25				X
3.50				
3.75				
4.0	X		X	

X = Recommended sizes for testing

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VIII. Performance Testing

The specific design characteristics of a device will determine the non-clinical testing that should be performed. Testing should ensure that the device design and construction are suitable for the intended use. We recommend you conduct the testing described below on completed catheters or suitable subassemblies. We recommend that you use product which has been exposed to a validated sterilization cycle or to a cycle validated to be equivalent if using smaller lots produced for clinical studies or during device development. Where appropriate, testing involving the balloon catheter should be done in an environment which simulates *in vivo* conditions (e.g., 37°C water or saline bath).

You should provide a complete report for each test conducted for our review. Each test report should include the information outlined in **Section VIII. Content and Format of Test Data** above. You should explain any omission, substitution, or combination of the tests outlined below. A tabular format is desirable; please see the example provided in **Appendix A**. We may also recommend additional testing to evaluate new designs or features of a device. Additionally, we recommend that you provide testing that compares your device to a currently legally marketed device.

A. Dimensional and Functional Attributes

1. Dimensional Verification

Significance

Accurate device dimensions help the physician to select proper product size. They may also affect the operator's ability to track the catheter to and across lesions.

Recommendation

We recommend that you provide dimensional specifications and tolerances for your device as manufactured. At a minimum, we recommend that you report effective length, shaft inner and outer diameter, and crossing profile.

The crossing profile is defined as the maximum diameter found between the proximal end of the balloon and the distal tip of the catheter. Testing should address potential differences in crossing profile that may exist in the circumferential direction. For these situations, we recommend that you evaluate the crossing profile of your catheter along different longitudinal paths (e.g., rotating the test

sample 90 degrees for measurements). We recommend that you report the crossing profile in the instructions for use, the outside package labeling, or both. We recommend the methods described in **ASTM F2081**[8] or their equivalents.

2. Balloon Preparation, Deployment and Retraction

Significance

The recommended instructions for use and techniques for preparation, deployment, and retraction, if properly followed, should safely and reliably deploy the balloon to the intended location without adversely affecting the device.

Recommendation

FDA recommends that you conduct testing to demonstrate that the balloon catheter can be safely and reliably prepared, deployed, and retracted using the recommended techniques, accessory devices, and instructions for use, without damage to the device. We recommend that this simulated use testing be performed by tracking the device through an *in vitro* fixture that mimics *in vivo* physiologic and anatomic conditions (e.g., a tortuous path, aqueous environment), to the length that would enter a patient in clinical use. For coronary indications, FDA recommends the tortuous path described by Figure X2.4 of **ASTM F2394**[9] or an equivalent. For peripheral indications, please provide the clinical basis for your final model. We recommend that you conduct testing with accessory devices that would be used in a typical clinical procedure (e.g., introducer or guiding catheter), using worst-case sizes (e.g., smallest guiding catheter ID). You should report any abnormality or difficulty observed during the simulated procedure, as well as any damage observed on the PTCA catheter or any of the accessory devices. We recommend that you measure and report the diameter and axial location of the largest deflated balloon profile (including the inner member or wire). This information can be used to determine the extreme dimensions of compatible accessory devices (i.e., minimum internal diameter), which should be identified in the labeling.

It may be possible to combine the Balloon Preparation, Deployment and Retraction testing with simulated use Coating Integrity testing (see Section 12 below) and Particulate Evaluation (see Section 13 below), but you should take care to ensure that only minimal additional handling of the sample is required for the coating integrity evaluation such that particulates are neither lost nor generated.

3. Balloon Rated Burst Pressure

Significance

The rated burst pressure (RBP) is the pressure at which 99.9% of balloons can survive with 95% confidence. Failure of a balloon to maintain integrity at the RBP could result in device failure or vessel damage.

Recommendation

FDA recommends that you conduct this testing on complete catheters or subassemblies in which the balloon is mounted on the catheter shaft. If the entire range of device sizes will have a single labeled RBP, we recommend that you conduct testing on the longest length of every balloon diameter and the shortest length of both the smallest diameter and largest diameter. Half and quarter sizes should also be tested. **Table 3** illustrates the recommended test matrix.

Table 3: PTCA Catheter Balloon Sizes recommended for RBP Testing

Balloon Diameter (mm)	Balloon Length (mm)			
	10	20	30	40
2.0	X			X
2.25				X
2.5				X
2.75				X
3.0				X
3.25				X
3.50			X	
3.75			X	
4.0	X		X	

*Table assumes a single labeled RBP

Additionally, we recommend that you test the balloon sizes as shown in **Table 3** for each different labeled RBP. We recommend that you test balloons that are not constrained by any test fixture such as tubing, and that you inflate the balloons incrementally until failure.

We recommend that you record as test failures any loss of:

- integrity of the balloon, such as a rupture or leak
- pressure due to failure of the balloon, shaft, or seals.

We recommend that you record the pressure at which the device failed and the failure mode. We also recommend that you calculate RBP as the pressure at which 99.9% of the balloons will survive with 95% confidence based on statistical analysis of the test data. We recommend that you specify RBP in the device labeling.

4. Balloon Fatigue (Repeat Balloon Inflations)

Significance

Balloons on PTCA catheters are often inflated multiple times during clinical use. Failure of the balloon to withstand multiple inflations could lead to device failure or vessel damage.

Recommendation

FDA recommends that you determine the repeatability, to 20 inflations, of successful balloon inflation to the RBP. We recommend that you test device sizes according to the "four corners" paradigm:

- largest diameter/longest length
- largest diameter/shortest length
- smallest diameter/longest length
- smallest diameter/shortest length.

We recommend that you test balloons that are not constrained by any test fixture such as tubing, and that you inflate the balloons incrementally until they reach the RBP. For each sample, we recommend that you hold the RBP for 30 seconds (or the time specified in the instructions for use), deflate the balloon, and inflate it again to the RBP, for a total of 20 cycles. We recommend that you report any loss of pressure, whether due to failure of the balloon, shaft, or proximal or distal seals, as a test failure. We recommend that you record all failure modes, and that your results demonstrate that 90% of the balloons will survive the test with at least 95% confidence.

We recommend 20 cycles for evaluation of PTCA catheters instead of the 10 cycles recommended for testing of stent delivery systems because repeat inflations of PTCA catheters are more likely in typical clinical use compared to stent delivery catheters.

5. Balloon Compliance (Diameter vs. Pressure)

Significance

The diameter of a deployed PTCA balloon varies with inflation pressure. A compliance chart in the labeling that relates balloon diameter to balloon pressure guides selection of catheter size to fit the target vasculature site. Incorrect selection of catheter size may lead to device failure or vessel damage.

Recommendation

FDA recommends that you test balloon sizes as illustrated in **Table 3**, and that you test multiple product lots. We recommend that you explain why you chose the test sample size. We recommend that you include data showing inflation pressure versus balloon diameter over the full range of recommended inflation diameters, and report the final results in the instructions for use, the outside package labeling, or both. A graphical or tabular presentation (i.e., a compliance chart) is desirable. We recommend that you identify the nominal inflation pressure and RBP, as shown in the example below. The compliance chart may include pressures up to (but not exceeding) 25% above the RBP, if you provide data and statistics demonstrating that 99% of the balloons will not fail at the listed pressure with 95% confidence. We also recommend that you describe how you performed any data rounding and show all instances. **Table 4** below shows an example of compliance chart for a balloon with 3.0 mm, 3.5 mm, and 4.0 mm diameters, with a RBP of 16 atmospheres (atm). (The nominal diameter occurs at 9.0 atm.)

Table 4: Balloon Compliance Example

Pressure (atm)	Balloon Nominal Diameter where x = balloon diameter at the given pressure		
	3.0 mm Balloon Diameter (mm)	3.5 mm Balloon Diameter (mm)	4.00 mm Balloon Diameter (mm)
9.0	X	X	X
10.0	X	X	X
11.0	X	X	X
12.0	X	X	X
13.0	X	X	X
14.0	X	X	X
15.0	X	X	X
16.0*	X	X	X

*RBP

6. Balloon Inflation and Deflation Time

Significance

Balloons occlude the target vessel and obstruct blood flow while inflated. Inflation and deflation times affect occlusion time. Excessively slow inflation or deflation of a balloon could lead to prolonged ischemia and damage to the myocardium.

Recommendation

FDA recommends that you demonstrate, using techniques recommended in your instruction manual (e.g., pre-dilation), that the balloon inflates and deflates within acceptable times, and provide the clinical basis for your acceptance criteria. We recommend that you test the largest diameter at the longest balloon length, and evaluate which other sizes to test. We also recommend you specify the balloon deflation times in your labeling.

7. Catheter Bond Strength

Significance

Failure of bonds in the catheter could lead to device failure or vessel damage.

Recommendation

FDA recommends that you test the bond strength at locations where adhesives, thermal fusion, or other joining methods are used for bonding components of the catheter. Prior to evaluating tensile strength, we recommend you precondition catheters by tracking through a tortuous path fixture (as described above in Section 2. Balloon Preparation, Deployment and Retraction). We recommend that testing demonstrate that all bonds can withstand tensile forces greater than those that may be experienced during clinical use. We also recommend you provide the clinical basis for your acceptance criteria.

8. Tip Pull Test

Significance

Failure of bonds in the distal tip could lead to device failure or vessel damage.

Recommendation

For devices with one or more joints in the distal tip (e.g., spring or nose-cone tips), FDA recommends that you determine the tensile force that will separate the distal tip from the catheter. We recommend that you precondition catheters prior to tip pull testing by tracking through a tortuous path fixture (as described above in Section 2. Balloon Preparation, Deployment and Retraction).

9. Flexibility and Kink Test

Significance

Catheters may be subjected to tight angulations in tortuous vasculature during use. Inability to withstand flexural forces that are typical of clinical use could lead to device failure or vessel damage.

Recommendation

FDA recommends that you conduct testing which demonstrates that the catheter will not kink at a bend radius that is appropriate for the intended anatomy. For example, we recommend that you consider wrapping the catheter around a series of mandrels with successively smaller radii until the catheter kinks or the lumen collapses. We also recommend you provide the clinical basis for your acceptance criteria.

10. Torque Strength

Significance

Catheters may be subjected to torsional forces during use. Even non-fixed wire catheters could be subject to torsional forces if the tip is inadvertently caught on a stent, calcified lesion, etc. Inability to withstand torsional forces that are typical of clinical use could lead to device failure or vessel damage.

Recommendation

FDA recommends that you measure the torque strength of the catheter when the distal tip is not free to rotate, by rotating the proximal end of the catheter until failure. We recommend that you precondition catheters prior to evaluating torque strength by tracking through a tortuous path fixture (as described above in Section 2. Balloon Preparation, Deployment and Retraction). We recommend that you report the number of rotations to failure and the failure mode for each sample tested. Additionally, we recommend that you test the catheter in a fixture that simulates the anatomy of the aortic arch and coronary arteries. We also recommend you provide the clinical basis for your acceptance criteria. We recommend that you report the number of turns to failure in the device labeling.

11. Radiopacity

Significance

Insufficient radiopacity may hamper safe and reliable delivery of the balloon to the intended location.

Recommendation

FDA recommends that you demonstrate that the radiopaque markers on the balloon catheter can be seen under typical fluoroscopic methods. We recommend that you provide a qualitative or quantitative indication of the visibility of the stent on real-time and plane film x-ray. It is acceptable to use data from images of animal implants, *in vitro* phantoms, or equivalent models.

12. Coating Integrity

Significance

Unintended delamination or degradation of a coating may lessen its benefit or otherwise negatively impact its clinical performance.

Recommendation

FDA recommends that you address the aspects described below for any coatings applied to the surfaces of your product.

Coating Description

We recommend that you describe the clinical purpose and intended function of the coating, such as enhanced radiopacity, thromboresistance, or lubricity.

We also recommend that you describe the physical structure of the coating, such as coating thickness, and indicate its chemical identification.

Test Samples

You should conduct all testing on the finished product subject to all manufacturing processes including sterilization. You should provide a scientific or statistical justification for the sample size for each test. We recommend that you implement a sampling plan to examine multiple lots of product (≥3) to assess both inter- and intra-lot variability. You should perform testing on the extremes and an appropriate intermediate size for the entire product matrix proposed (*four corners and intermediate* size matrix — see **Table 5** below).

Table 5: Example of *Four Corners and Intermediate* Size Matrix

		Length (mm)						
		8	11	15	18	21	24	27
Diameter (mm)	2.5	X						X
	3.0				X			
	3.5							
	4.0	X						X

It may be possible to combine the simulated use Coating Integrity (see below) and Particulate Evaluation (see Section 13 below) with Balloon Preparation, Deployment and Retraction testing (see Section 2 above), but you should take care to ensure that only minimal additional handling of the sample is required for the coating integrity evaluation such that particulates are neither lost nor generated.

Interpretation of Data

Coating integrity is considered a characterization test. Acceptance criteria are not required; however, you should provide an interpretation of the data.

In your coating integrity test reports you should include a detailed discussion of the surfaces using any practical methods to quantify defects. This may include counting the number of total defects per unit area, measuring representative defect areas, and measuring worst-case defect areas. You should support your discussion with representative images (including worst-case) at a sufficient magnification to characterize the defects. Multiple magnifications may be needed to visualize and adequately characterize the product. The discussion of acceptable coating integrity should include a justification that the number and size of defects observed will not impact clinical performance.

FDA recommends that you address the aspects described below for any coatings applied to the surfaces of your product.

Baseline Coating Integrity

FDA recommends that you conduct a visual assessment of the coating integrity on all appropriate surfaces of the catheter before expansion to establish a baseline for comparison to coating characteristics after testing performed under other conditions. We recommend that you appropriately quantify characteristics such as continuity and voids in the coating, as described above.

Simulated Use Coating Integrity

FDA also recommends that you evaluate the coating integrity after simulated use, via visual assessment. Catheters should be tracked through a tortuous path fixture (as described above in Section 2. Balloon Preparation, Deployment and Retraction) and then expanded in air or an aqueous medium to the maximum labeled diameter described in the Instructions for Use prior to visual inspection.

We recommend you test coating integrity under the worst-case conditions of use. For example, for balloons intended for ISR or post-deployment stent expansion, we recommend that you evaluate the coating integrity after tracking the device through a tortuous path fixture (as described above in Section 2. Balloon Preparation, Deployment and Retraction) and inflating to the largest labeled diameter within a stent which has been deployed in the mock vessel.

13. Particulate Evaluation

Significance

Particulate matter can be generated by the manufacturing process or from the breakdown of any coating (e.g., hydrophilic coating) on the catheter or from the device packaging. If particles are introduced in the bloodstream during an angioplasty procedure, they may present an embolic risk to the patient. Measurement of the total quantity and size of particulates a device may generate is an indication of embolic risk.

Recommendation

We recommend that you measure the total quantity and size of the particulates generated during the simulated use of your device.

Test Samples

You should conduct all testing on the finished product subject to all manufacturing processes including sterilization. You should provide a scientific or statistical justification for the sample size you plan to test. We recommend that you implement a sampling plan to examine multiple lots of product (≥3) to assess both inter- and intra-lot variability. You should perform testing on the extremes and an appropriate intermediate size for the entire product matrix proposed (*four corners and intermediate* size matrix — see **Table 5** above).

It may be possible to combine the Particulate Evaluation (see below) and simulated use Coating Integrity testing (see Section 12 above) with Balloon Preparation, Deployment and Retraction testing (see Section 2 above), but you should take care to ensure that only minimal additional handling of the sample is required for the coating integrity evaluation such that particulates are neither lost nor generated.

Interpretation of Data

Particulate generation is considered a characterization test. Acceptance criteria are not required; however, you should provide an interpretation of the data.

Test Methods

We recommend that you evaluate particulate generated by the entire PTCA system, including accessory devices expected to be used during a clinical procedure. Catheters should be tracked through a tortuous path fixture (as described above in Section 2. Balloon Preparation, Deployment and Retraction) and then expanded in an aqueous medium to the maximum labeled diameter described in the Instructions for Use prior to visual inspection. When deployed, the balloon should be in direct contact with the simulated vessel without the use of other coatings, lubricants, sheaths, or protective wraps between the balloon and the simulated vessel. To ensure measurement of the total number of particles that could be potentially introduced into the bloodstream, the catheter should be inserted into the text fixture to the extent at which it would be inserted in clinical use. The total number of particulates including those from the catheter and accessory devices should be

reported in each of three size ranges: ≥10µm, ≥25µm, and at the largest size for which validation yields ≥75% recovery. At a minimum, the largest size should be ≥50µm. Appropriate precautions should be taken to ensure that the particles are suspended during sampling for particle counting and sizing to minimize artifacts from the test system.

We recommend you perform particulate evaluation under the worst-case conditions of use. For example, for balloons intended for ISR or post-deployment stent expansion, we recommend that you evaluate the quantity and sizes of particulate generated from tracking the device through the tortuous path fixture (as described above in Section 2. Balloon Preparation, Deployment and Retraction) and inflating to the largest labeled diameter within a stent which has been deployed in the mock vessel.

Method Validation

You should describe and validate particle counting and sizing methods. We recommend that you introduce a known amount of various particle sizes into the test setup and quantify the amount of particles recovered. The number of particles recovered should closely approximate the number you artificially introduced into the system. For a system to be considered validated, ≥90% recovery should be demonstrated for the ≥10µm and ≥25µm size ranges.

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B. Additional Tests for Catheters Intended for Infusion of Contrast Media or Other Fluids

1. Catheter Body Burst Pressure

Significance

The catheter body should be designed to withstand pressures typically needed to achieve contrast media flow rates used in clinical practice. Inability to withstand pressures that are typical of clinical use could lead to device failure or vessel damage.

Recommendation

FDA recommends that you determine the maximum pressure that the catheter body can withstand during injection. We recommend you conduct the testing under clinical use conditions, i.e., including use of a syringe, automatic injector, etc. The contrast medium or fluid should be representative of worst case clinical conditions. We also recommend you provide the clinical basis for your acceptance criteria.

2. Contrast Media Flow Rate

Significance

The catheter should be designed to achieve clinically acceptable contrast media flow rates. Inability to achieve acceptable flow rates could lead to user error and adverse clinical consequences.

Recommendation

FDA recommends that you conduct testing that demonstrates that the catheter is capable of achieving clinically acceptable contrast media flow rates. We recommend that testing be done at maximum catheter burst pressures (as identified in the test described above), as well as pressures typical of clinical use. We recommend that you report the maximum flow rate in the device labeling. We also recommend you provide the clinical basis for your acceptance criteria.

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C. Additional Tests for Catheters Intended for In-Stent Restenosis or for Stent Expansion following Stent Deployment

If you label a PTCA catheter for in-stent restenosis, or for stent expansion immediately following stent deployment (for purposes of securing the stent to the vessel wall and ensuring that the stent is completely deployed), we recommend you conduct the following tests within an expanded stent.

1. Balloon Rated Burst Pressure (in Stent)

Significance

The rated burst pressure (RBP) is the pressure at which 99.9% of balloons can survive with 95% confidence. Use of a PTCA catheter inside a stent may have an effect on the RBP. Failure of a balloon to maintain integrity at the RBP could result in device failure or vessel damage.

Recommendation

We recommend that you conduct this testing on complete catheters or subassemblies in which the balloon is mounted on the catheter shaft. We recommend that you conduct testing on representative sizes as shown in the example in **Table 3**, for each labeled RBP. We recommend that you inflate the balloons incrementally until failure.

We recommend that you record as test failures any loss of:

- integrity of the balloon, such as a rupture or leak
- pressure due to failure of the balloon, shaft, or seals.

We recommend that you record the pressure at which the device failed and the failure mode. We also recommend that you calculate RBP as the pressure at which 99.9% of the balloons will survive with 95% confidence based on statistical analysis of the test data. We recommend that you specify RBP in the device labeling.

2. Balloon Fatigue (Repeat Balloon Inflations; in Stent)

Significance

Balloons on PTCA catheters are often inflated multiple times during clinical use. Use of a PTCA catheter inside a stent may affect balloon fatigue strength. Failure of the balloon to withstand multiple inflations could lead to device failure or vessel damage.

Recommendation

FDA recommends that you determine the repeatability, to 10 inflations, of successful balloon inflation to the RBP. We recommend that you test device sizes according to the "four corners" paradigm:

- largest diameter/longest length
- largest diameter/shortest length
- smallest diameter/longest length
- smallest diameter/shortest length.

We recommend that you inflate the balloons incrementally until they reach the RBP. For each sample we recommend that you hold the RBP for 30 seconds (or the time specified in the instructions for use), deflate the balloon, and inflate it again to the RBP, for a total of 10 cycles. We recommend that you report any loss of pressure, whether due to failure of the balloon, shaft, or proximal or distal seals, as a test failure. We recommend that you record all failure modes, and that your results demonstrate that 90% of the balloons will survive the test with at least 95% confidence.

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IX. Animal Testing

For devices with notable dissimilarity from legally marketed PTCA devices (e.g., new indications, designs, or technology), we recommend that you conduct preclinical testing in animals to confirm safety of the procedure, to evaluate the functional characteristics of the device design and to validate the performance of other interventional cardiovascular devices used in conjunction with the PTCA catheter. We recommend that you evaluate PTCA devices in an appropriate animal model that closely approximates the intended use of the device in humans, and that you provide this

information in your submission. We encourage you to contact the review branch early in the product development process to discuss your study design. General provisions for animal testing of PTCA devices are discussed below.

Device

We recommend that you use the finished, sterilized devices including the delivery catheters in your studies. Studies should include a reasonable representation of all device sizes.

Control

We recommend that you consider the inclusion of a control device to facilitate evaluation of the histopathology results. A PTCA catheter currently marketed in the U.S. is one example of an appropriate control device.

Acute Observations

We recommend that preclinical animal testing address:

- damage to vessel wall
- potential to cause thrombosis or hemolysis over the course of the procedure
- angiographic assessment during procedures, including evaluation of flow rate, thrombus formation and vessel injury.

Follow-Up Observations

We recommend the animal studies include 4-6 follow up observations with detailed pathology at 24 to 48 hours post-treatment as described below.

Pathology

We recommend that the evaluations performed on necropsied animals include gross assessment of the device as well as careful histological examination of the vessel segment where the device was deployed. The vessel segment should be examined for vessel injury and inflammation. The animal study report should include the full pathology report, providing line listings and clear copies of photographs and photomicrographs.

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X. Clinical Information

The agency will rely upon well-designed bench and/or animal testing rather than requiring clinical studies for new devices unless there is a specific justification for asking for clinical information to support a determination of substantial equivalence. While, in general, clinical studies will not be needed for most PTCA devices, FDA may recommend that you collect clinical data for a PTCA device with any one of the following:

- indications for use dissimilar from legally marketed PTCA device of the same type
- designs dissimilar from designs previously cleared under a premarket notification
- new technology; i.e., technology different from that used in legally marketed PTCA devices
- sizes not previously marketed.

FDA will always consider alternatives to clinical testing when the proposed alternatives are supported by an adequate scientific rationale.

If you conduct a clinical study, your study design should address the concerns described below. We recommend you contact the review branch early in your device development process to discuss the study design appropriate to your device.

Study Design

We recommend that you conduct a multi-center, prospective single-arm study designed to collect data to support the safety and effectiveness of your device. For devices that will be indicated for use for in-stent restenosis, your study should include a sufficient number of in-stent restenosis patients.

Primary Safety Endpoint(s)

We recommend that your study include a primary safety endpoint such as acceptable rates for in-hospital and out-of-hospital complications. Complications are typically defined as clinically significant major adverse cardiac events (MACE) including death, myocardial infarction (MI, Q-wave and non-Q-wave), coronary artery bypass graft (CABG) surgery, and repeat target vessel revascularization.

Primary Efficacy Endpoint(s)

We recommend that your study include a primary efficacy endpoint such as a clinically meaningful decrease in post-procedure percent diameter stenosis. This endpoint is typically assessed by collecting and analyzing qualitative and quantitative angiographic data recorded both by the physician during the procedure and by post-procedure independent core lab analysis.

If a clinical study is needed to demonstrate substantial equivalence, i.e., conducted prior to obtaining 510(k) clearance of the device, and will be conducted in the United States, the study must be conducted under the Investigational Device Exemptions (IDE) regulation, 21 CFR Part 812. We believe that the PTCA device addressed by this guidance document is a significant risk device as defined in 21 CFR 812.3(m)(4).**[10]** In addition to the requirement of having an FDA-approved IDE, sponsors of such trials must comply with the regulations governing institutional review boards (21 CFR Part 56) and informed consent (21 CFR Part 50).

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XI. Sterilization and Shelf Life

A. Sterilization

FDA recommends that you provide sterilization information in accordance with the **Updated 510(k) Sterility Review Guidance K90-1; Final Guidance for Industry and FDA**.**[11]** You should sterilize the device to a sterility assurance level (SAL) of 1 x 10^{-6} using a sterilization cycle that has been validated in accordance with the Quality System Regulation.

PTCA catheters are devices in contact with circulating blood; therefore we recommend you test the devices for pyrogenicity. We recommend that you consider pyrogenic responses to gram-negative bacterial endotoxin using a standard method, such as those outlined in the **USP 28 <85> Bacterial Endotoxin Limulus Amoebocyte Lysate (LAL) Test**, or an equivalent method. We recommend that your specifications include the test procedure and acceptance criteria for endotoxins. All blood-contacting cardiovascular devices and combination products should be pyrogen-free. Pyrogenicity testing is used to help define limits to protect patients from the risk of febrile reaction. We also recommend you provide a:

- description of the method used to make the determination, e.g., limulus amebocyte lysate (LAL);
- identification of the testing endpoint reached and rationale for selecting that endpoint;
- description of the extraction technique used to obtain the test fluid from the test device, showing that all clinically relevant contact surfaces of the test device were assessed and;
- identification of the reference method used, e.g., USP, ANSI/AAMI ST 72, or FDA guidance.

B. Shelf Life

FDA recommends that shelf life testing address package integrity to ensure sterility, as well as stable device functionality over the expected life cycle.

To evaluate device functionality, we recommend that you assess each of the bench tests described in **Section IX.** and repeat all tests that evaluate design characteristics affected by aging. For example, aging can potentially affect the performance of polymer materials used for PTCA balloons, catheters, and coatings; therefore, all tests other than radiopacity should be repeated after aging. We also recommend that you provide the protocol used for your shelf life testing, the results of the testing, and the conclusions drawn from your results.

If you use devices subjected to accelerated aging for shelf life testing, we recommend that you specify the way in which the device was aged. Since PTCA catheters generally contain polymeric materials, you should plan to conduct real-time testing to confirm that accelerated aging is reflective of real-time aging. This testing should be conducted in parallel with 510(k) review and clearance, with results documented-to-file (i.e., these results do not need to be submitted to FDA).

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XII. Labeling

The premarket notification must include labeling in sufficient detail to satisfy the requirements of 21 CFR 807.87(e). The following suggestions are aimed at assisting you in preparing labeling that satisfies the requirements of 21 CFR Part 801.**[12]**

We recommend that you include the following items in the labeling for all PTCA devices, modifying as appropriate for specific catheter designs. If you do not include any of these items, we recommend you explain your rationale in your submission.

Device name

We recommend that you include both brand name and generic device name.

Description

We recommend that you include a description of the catheter identifying the important components and the functions of each.

Indications for Use

The indications for use described in the labeling should be supported by appropriate information in the 510(k) submission. An example of an indications for use statement is as follows:

The device is indicated for:

- balloon dilatation of a hemodynamically significant coronary artery or bypass graft stenosis in patients evidencing coronary ischemia for the purpose of improving myocardial perfusion

- treatment of acute myocardial infarction
- in-stent restenosis, and/or
- post-deployment stent expansion.

Contraindications

Labeling should indicate this device is contraindicated for treatment of the unprotected left main coronary artery and for coronary artery spasm in the absence of a significant stenosis.

Warnings

In addition to anywarnings specific to your type of PTCA device,the labeling should address sterilization, selection of appropriate balloon diameter, treatment of special populations, procedures for manipulating the balloon, RBP, and the inflation medium, for example:

This device is intended for single use only. Do not resterilize and/or reuse it, as this can potentially result in compromised device performance and increased risk of cross-contamination.

To reduce the potential for vessel damage, the inflated diameter of the balloon should approximate the diameter of the vessel just proximal and distal to the stenosis.

PTCA in patients who are not acceptable candidates for coronary artery bypass graft surgery warrants careful consideration, including possible hemodynamic support during PTCA, as treatment of this patient population carries special risk.

When the catheter is exposed to the vascular system, it should be manipulated while under high-quality fluoroscopic observation. Do not advance or retract the catheter unless the balloon is fully deflated under vacuum. If resistance is met during manipulation, determine the cause of the resistance before proceeding.

Balloon pressure should not exceed the rated burst pressure. The rated burst pressure is based on the results of *in vitro* testing. At least 99.9 percent of the balloons, (with a 95 percent confidence) will not burst at or below their rated burst pressure. Use of a pressure monitoring device is recommended to prevent over-pressurization.

To reduce the potential for air embolus into the vessel, use only the recommended balloon inflation medium. Never use air or any gaseous medium to inflate the balloon.

Precautions

In addition to anyprecautionsspecific to your type of PTCA device,the labeling should advise users to use the product prior to expiration, to verify functionality before use, and that the device should only be used by physicians trained in PTCA, for example:

Use the catheter prior to the: "Use Before" date specified on the package.

Before angioplasty, the catheter should be examined to verify functionality and ensure that its size and shape are suitable for the specific procedure for which it is to be used.

The catheter system should be used only by physicians trained in percutaneous transluminal coronary angioplasty.

Labeling should also include a precaution about the administration of recommended anticoagulant and vasodilator therapy, if not included in the Directions for Use section.

For balloons that have not been cleared for the treatment of ISR, labeling should advise the safety and effectiveness of this use have not been established, for example:

The safety and effectiveness of this PTCA balloon catheter for the treatment of ISR has not been established.

For balloons that have not been cleared for stent expansion, the labeling should address the exclusion of that indication from the intended use, for example:

This balloon is not intended for the expansion or delivery of a stent.

In cases where FDA determines that there is a reasonable likelihood that the device will be used for an intended use not identified in the proposed labeling for the device and that such use could cause harm, FDA may determine that limitations as described under 513(i)(1)(E) are necessary.

Adverse Effects

If a clinical study was performed to support the submission, labeling should list the adverse events observed, along with a brief narrative statement about the source of each.

Possible adverse effects include, but are not limited to, the following:

- death
- acute myocardial infarction
- acute vessel closure
- total occlusion of the coronary artery or bypass graft
- coronary vessel dissection, perforation, rupture or injury
- restenosis of the dilated vessel
- hemorrhage or hematoma
- unstable angina

- arrhythmias, including ventricular fibrillation
- drug reactions, allergic reaction to contrast medium
- hypotension
- hypertension
- infection
- coronary artery spasm
- arteriovenous fistula
- stroke, air embolism and embolization or fragmentation of thrombotic or athlerosclerotic material.

Clinical Studies (if performed)

If a clinical study was performed to support the submission, we recommend that you include a summary of the experience, including:

- purpose
- conclusions
- study design
- results.

Directions for Use

As a prescription device, under 21 CFR 801.109, the device is exempt from having adequate directions for lay use. Nevertheless, under 21 CFR 807.87(e), we recommend submitting clear and concise instructions that delineate the technological features of the specific device and how the device is to be used on patients. Instructions should encourage local/institutional training programs designed to familiarize users with the features of the device and how to use it in a safe and effective manner.

We recommend that you provide specific instructions for use of the PTCA device. We recommend that you state the rated burst pressure (RBP) of the balloon. For PTCA devices intended for infusion of contrast media or other fluids, we also recommend that you state the catheter body burst pressure. We recommend that you indicate the deflated balloon profile in the instructions for use, the outside package labeling, or both. We recommend that you include balloon compliance data which shows how balloon diameter varies as a function of inflation pressure. A tabular or graphical representation is desirable.

For post-deployment stent expansion:

In addition to the above labeling provisions, we recommend that the device labeling also include the following statements:

The subject device was tested on the bench with the [brand name] stent.

All stents should be deployed in accordance with the manufacturer's indications and instructions for use.

Revision Date

We recommend that you include the date of modified labeling.

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Appendix A: Test Summary

Test		Sizes Tested and Sample Sizes	Test Method or Standard Reference	Accept/Reject Criteria	Results
Dimensional and Functional Attributes	Dimensional Verification				
	Balloon Preparation, Deployment and Retraction				
	Balloon Rated Burst Pressure (RBP)				
	Balloon Fatigue (Repeat Balloon Inflations)				
	Balloon Compliance (Diameter vs. Pressure)				
	Balloon Inflation and Deflation Time				
	Catheter Bond Strength				
	Tip Pull Test				

	Flexibility a nd Kink Test				
	Torque Strength Test				
	Radiopacity				
	Coating Integrity				
	Particulate Evaluation				
Additional Tests for Catheters Intended for Infusion of Contrast Media or Other Fluids	Catheter Body Burst Pressure				
	Contrast Media Flow Rate				
Additional Tests for Catheters Intended for In Stent Restenosis for Stent Expansion following Stent Deployment	Balloon Rated Burst Pressure (RBP; in Stent)				
	Balloon Fatigue (Repeat Balloon Inflations; in Stent)				

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Appendix B: Applicable Standards

A list of FDA-recognized standards is available at **http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm)**

ISO Standards

10993 Biological Evaluation of Medical Devices

11134 Sterilization of health care products – Requirements for validation and routine control – industrial moist heat sterilization

11135 Medical Devices - Validation and Routine Control of Ethylene Oxide Sterilization

11137 Sterilization of health care products – Requirements for validation and routine control – radiation sterilization and ANSI/AAMI/ISO 11137:1994 (Amendment 1:2002)

11607 Packaging for terminally sterilized medical devices

11737 Sterilization of medical devices – microbiological methods

·Part 1 – Estimation of the population of microorganisms on product

·Part 2 – Tests of sterility performed in the validation of a sterilization process

·Part 3 – Guidance on evaluation and interpretation of bioburden data

14161 Sterilization of health care products – Biological indicators – Guidance for the selection, use and interpretation of results, 2ed. (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/Detail.CFM?STANDARD__IDENTIFICATION_NO=15177)

14937 Sterilization of Health Care Products - General Requirements for Characterization of a Sterilizing Agent and the Development,

Validation, and Routine Control of a Sterilization Process for Medical Devices

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ASTM Standards

F1984-99 (2003) Whole Complement Activation in Serum by Solid Materials

F2081 Standard Guide for Characterization and Presentation of the Dimensional Attributes of Vascular Stents

F2065-00e1 Alternative Pathway Complement Activation in Serum by Solid Materials

F2394 Standard Guide for Measuring Securement of Balloon Expandable Vascular Stent Mounted on Delivery System

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[1] Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)'s (Aug. 2005), available at: **http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084396.pdf (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084396.pdf)**

[2] How to Prepare a 510(k) Submission **http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/default.htm**

(http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/default.htm).

[3] See **http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080735.htm (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080735.htm)**. You may access a list of the FDA-recognized sections of ISO 10993 from the FDA website at: **http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm)**.

[4] ASTM F2065-00e1 Alternative Pathway Complement Activation in Serum by Solid Materials.

[5] ASTM F1984-99 (2003) Whole Complement Activation in Serum by Solid Materials.

[6] FDA acknowledges that ISO 10993-1 does not recommend consideration of genotoxicity testing for materials in contact with circulating blood with limited contact duration (less than 24 hours). Per FDA's Blue Book Memorandum #G95-1, 'Use of International Standard ISO 10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing', recommendations outlined in ISO 10993-1 should be considered in concert with FDA's Blue Book Memorandum #G95-1. The test matrix outlined in Blue Book Memorandum #G95-1 Table 1 indicates that genotoxicity is an additional test which may be applicable for materials in contact with circulating blood with limited contact duration (less than 24 hours).

[7] The branch is available to discuss your protocol with you. See also the section entitled **IDE Approval Process** in **CDRH Device Advice** at: **http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/ InvestigationalDeviceExemptionIDE/ucm046164.htm#pre_ide (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046164.htm#pre_ide)**.

[8] ASTM F2081 Standard Guide for Characterization and Presentation of the Dimensional Attributes of Vascular Stents

[9] ASTM F2394 Standard Guide for Measuring Securement of Balloon Expandable Vascular Stent Mounted on Delivery System

[10] See Information Sheet Guidances: Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors, available at **http://www.fda.gov/oc/ohrt/irbs/devices.html#risk (http://www.fda.gov/oc/ohrt/irbs/devices.html#risk)**.

[11] Updated 510(k) Sterility Review Guidance K90-1; Final Guidance for Industry and FDA (Aug. 2002), available at: **http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm072783.htm (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm072783.htm)**

[12] Although final labeling is not required for 510(k) clearance, final labeling must comply with the requirements of 21 CFR 801 before a medical device is introduced into interstate commerce. In addition, final labeling for prescription medical devices must comply with 21 CFR 801.109. Labeling provisions in this guidance are consistent with the requirements of Part 801.

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More in Guidance Documents (Medical Devices and Radiation-Emitting Products) (/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm)

Cross-Center Final Guidance (/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm081752.htm)

Office of Compliance Final Guidance (/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070269.htm)

Office of the Center Director Final Guidance (/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm110228.htm)

Office of Communication and Education Final Guidance (/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070271.htm)

Office of Device Evaluation Final Guidance 2010 - 2016 (/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm198577.htm)

Office of Device Evaluation Final Guidance 1998 - 2009 (/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070272.htm)

Office of Device Evaluation Final Guidance 1976 - 1997 (/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080283.htm)

Office of In Vitro Diagnostics and Radiological Health Final Guidance (/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070274.htm)

Office of Surveillance and Biometrics Final Guidance (/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070275.htm)

Office of Science and Engineering Laboratories Final Guidance (/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070277.htm)

Draft Guidance (/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm407274.htm)

Radiation-Emitting Products Guidance (/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm283507.htm)

Withdrawn Guidance (/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm425025.htm)