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Metal Expandable Biliary Stents - Premarket Notification (510(k)) Submissions

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

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You should submit comments and suggestions regarding this draft document within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions about this document, contact the Division of Reproductive, Gastro-Renal, Urological Devices at 301-796-7030.

When final, this guidance will supersede "Guidance for the Content of Premarket Notifications for Metal Expandable Biliary Stents," issued on February 5, 1998.

FDA U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR DEVICES & RADIOLOGICAL HEALTH

U.S. Department of Health and Human Services
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Preface

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Metal Expandable Biliary Stents - Premarket Notification (510(k)) Submissions

Draft Guidance for Industry and Food and Drug Administration Staff

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. Introduction

This draft guidance document provides draft recommendations for 510(k) submissions for metal expandable biliary stents and their associated delivery systems. These devices are intended to provide luminal patency of the biliary tree. This guidance is issued for comment purposes only.

For the current edition of the FDA-recognized standard(s) referenced in this document, see the FDA Recognized Consensus Standards Database Web site at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfstandards/search.cfm. For more information regarding use of consensus standards in regulatory submissions, please refer to FDA guidance titled "Recognition and Use of Consensus Standards."[1]

FDA's guidance documents, including this draft guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance means that something is suggested or recommended, but not required.

II. Background

This draft guidance, when final, will supersede the guidance "Guidance for the Content of Premarket Notifications for Metal Expandable Biliary Stents," issued on February 5, 1998.[2] FDA is updating this guidance to reflect current review practices.

[1] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm077295.pdf

[2] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm080201.pdf

Since 1998, FDA has placed limitations on substantial equivalence determinations for biliary stents pursuant to section 513(i)(1)(E) of the Federal Food, Drug, and Cosmetic Act (FD&C Act). For each, FDA determined that there is a reasonable likelihood that the device will be used in the vascular system, which is an intended use not identified in the proposed labeling, and that such use could cause harm. This is due to a lack of safety and effectiveness data, including clinical data, about the use of biliary stents in the vasculature. This includes safety (failure modes) and effectiveness concerns specific to the vascular use of stents that are not assessed for biliary applications, e.g., vascular restenosis, stent fracture if placed across a joint, and long-term fatigue testing. While metallic stents have since been approved for specific cardiovascular indications, the Agency continues to have safety and effectiveness concerns about use of biliary stents for vascular applications, unless the device has also been approved for a vascular indication through a separate premarket approval application. Therefore, in most cases, FDA continues to place limitations on substantial equivalence determinations for biliary stents (see sections V.I(1) Display of Common Name and Trade Name and V.I(4) Warnings), and modifications to biliary stents are not eligible to be reviewed under the Special 510(k) paradigm.

This document supplements other FDA documents regarding the specific content requirements and recommendations of a premarket notification (510(k)) submission. You should also refer to 21 CFR 807.87 and FDA's guidance, "Format for Traditional and Abbreviated 510(k)s."[3]

III. Scope

The scope of this guidance is limited to metal expandable biliary stents regulated under 21 CFR 876.5010 (Biliary catheter and accessories) and with product code FGE (Catheter, Biliary, Diagnostic). This guidance applies only to biliary stents indicated for palliation of malignant strictures in the biliary tree. It does not apply to biliary stents indicated to treat benign strictures or stents intended to be used in the vasculature, tracheal/bronchial tubes, or other gastrointestinal anatomy.

IV. Definitions

For the purposes of this guidance, the following definitions are utilized.

Biliary stent: An expandable biliary catheter, constructed either wholly or partially of metal, that may be uncovered, partially covered, or fully covered. The biliary stent is implanted in the biliary tree and used to provide palliation of malignant strictures.

Balloon expandable stent: A biliary stent that is expanded by a balloon catheter. The diameter of the stent increases as the balloon diameter increases. The stent remains expanded after deflation of the balloon.

Self-expanding stent: A biliary stent that expands automatically after being released from a stent delivery system (e.g., a catheter); i.e., it does not require balloon inflation or other

[3] https://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm084365.htm

mechanical assistance to expand. The self-expanding quality can result from material properties, geometry, or both.

Stent delivery system (SDS): A system that delivers a biliary stent to a target site within the bile duct and then deploys the stent. A stent delivery system for a balloon expandable stent consists of a balloon catheter. Self-expanding stent delivery systems do not typically include a balloon.

V. Premarket Submission Recommendations

A. Device Description

We recommend that you identify your device using the regulation and product code described in **Section III above**. For each model of biliary stent you propose to market, you should include the following information:

- labeled diagram, photograph, or schematic drawing;
- stent specifications including the length and diameter;
- description and diagram of the stent geometry, including strut width and thickness;
- a detailed description of the SDS, including the working length, how the stent is mounted, as well as identification and description of any other devices provided with the stent. You should indicate whether the stent is to be placed endoscopically or percutaneously; and
- an explanation if any of the device components are disposable or reusable.

B. Predicate Comparison

For devices reviewed under the 510(k) process, manufacturers must compare their new device to a similar legally marketed predicate device to support its substantial equivalence (section 513(i) (21 U.S.C. 360c(i)) of the FD&C Act; 21 CFR 807.87(f)). This comparison should provide information to show how your device is similar to and different from the predicate. Side by side comparisons, whenever possible, are desirable. See **Table 1** below for an example of how this information may be organized.

Table 1: Example of a Device and Predicate Comparison

CHARACTERISTIC	DEVICE	PREDICATE DEVICE
510(k) number	This submission	Kxxxxxx
Indications for use statement		
Expansion method		
Stent material		
Method of introduction		
Sterility		
Delivery system length		
Stent lengths		
Stent diameters		
Stent geometry	Strut length: Strut width: Woven cell dimensions:	Strut length: Strut width: Woven cell dimensions:
Delivery system profile		
Performance specifications (see **Section V.G below** of this guidance)		

C. Biocompatibility

Significance: Biliary stents contain patient-contacting materials, which, when used for their intended purpose (i.e., contact type and duration), may induce a harmful biological response.

Recommendation: You should determine the biocompatibility of all patient-contacting components in your biliary stent and SDS. If your device is identical in composition and processing to biliary stents and/or SDSes with a history of successful use, you may reference previous testing experience or literature, if appropriate. For some device materials, it may be appropriate to provide a reference to either a recognized consensus standard, or to a Letter of Authorization (LOA) for a device Master File (MAF).

If you are unable to identify a legally marketed predicate device with similar location/duration of contact and intended use that uses the same materials as used in your device, we recommend you conduct and provide a biocompatibility risk assessment. The assessment should explain the relationship between the identified biocompatibility risks, the information available to mitigate the identified risks, and identify any knowledge gaps that remain. You should then identify any biocompatibility testing or other evaluations that were conducted to mitigate any remaining risks.

We recommend that you follow FDA's guidance "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process,'"[4] which identifies the types of biocompatibility assessments that should be considered and recommendations regarding how to conduct related tests.

[4] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm348890.pdf

Per ISO 10993-1: *Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process* and Attachment A of FDA's guidance on ISO-10993-1, biliary stents are implant devices in permanent contact with tissue/bone. Therefore, we recommend the following biocompatibility endpoints be addressed in your biocompatibility evaluation:

- cytotoxicity;
- sensitization;
- irritation or intracutaneous reactivity;
- acute systemic toxicity;
- material-mediated pyrogenicity;
- subacute/subchronic toxicity;
- chronic toxicity; and
- implantation.

Per ISO 10993-1: *Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process* and Attachment A of FDA's guidance on ISO-10993-1, SDSes are considered to have limited duration contact with mucosal membrane (endoscopic delivery) or breached tissue (percutaneous transhepatic delivery). Therefore, we recommend the following biocompatibility endpoints be addressed in your biocompatibility evaluation:

- cytotoxicity;
- sensitization;
- irritation or intracutaneous reactivity;
- acute systemic toxicity (percutaneous transhepatic delivery only); and
- material-mediated pyrogenicity (percutaneous transhepatic delivery only).

The following additional considerations are recommended for biliary stents:

- As it may affect the biocompatibility of the device, you should provide information on specific stent processing steps, including heat treatment and any subsequent surface finishing steps that may be employed.

- Differences in formulation, processing, sterilization, or device surface properties (e.g., nano-structuring) that could affect biocompatibility of the final product may warrant additional biocompatibility testing.

D. Sterility

Significance: A biliary stent and associated SDS should be adequately sterilized to minimize infections and related complications.

Recommendation: For biliary stents and associated SDSes labeled as sterile, we recommend that you provide information for the final device in accordance with FDA's guidance "Submission

and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile."[5]

E. Shelf Life and Packaging

Significance: Shelf-life testing is conducted to support the proposed expiration date through evaluation of the package integrity for maintaining device sterility and/or evaluation of any changes to device performance or functionality.

Recommendation: With respect to package integrity for maintaining device sterility, you should provide a description of the packaging, including how it will maintain the device's sterility, and a description of the package integrity test methods, but not the package test data. We recommend that package integrity test methods include simulated distribution and associated package integrity, as well as simulated (and/or real-time) aging and associated seal strength testing, to validate package integrity and shelf life claims. We recommend you follow the methods described in the FDA-recognized series of consensus standards AAMI/ANSI/ISO 11607-1: *Packaging for terminally sterilized medical devices – Part 1: Requirements for materials, sterile barrier systems and packaging* and AAMI/ANSI/ISO 11607-2: *Packaging for terminally sterilized medical devices – Part 2: Validation requirements for forming, sealing and assembly processes.*

With respect to evaluating the effects of aging on device performance or functionality, shelf-life studies should evaluate critical device properties to ensure that it will perform adequately and consistently during the entire proposed shelf life. To evaluate device functionality, we recommend that you assess each of the bench tests described in **Section V.G below** and repeat all tests that evaluate design components or characteristics that are potentially affected by aging.

We recommend that you provide a summary of the test methods used for your shelf life testing, results and the conclusions drawn from your results. If you use devices subject to accelerated aging for shelf life testing, we recommend that you specify the way in which the devices were aged. We recommend that you age your devices as per the currently FDA recognized version of ASTM F1980: *Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices* and specify the environmental parameters established to attain the expiration date. For devices or components containing polymeric materials, you should plan to conduct testing on real-time aged samples to confirm that the 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 in the design history file (i.e., complete test reports do not need to be submitted to FDA).

[5] https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm109897.pdf

F. Magnetic Resonance (MR) Compatibility for Passive Implants

Significance: MR imaging of patients with biliary stents poses the following potential hazards:

- movement of the stent, resulting in tissue damage or displacement of the stent;
- heating of the tissue surrounding the stent, resulting in damage to the biliary duct and surrounding tissue; and
- image artifacts near the stent that may render MR images of nearby anatomy uninterpretable or misleading.

Recommendation: We recommend that you address the issues affecting the safety and compatibility of your biliary stent in the MR environment as described in the "Guidance for Industry and FDA Staff: Establishing Safety and Compatibility of Passive Implants in the MR (Magnetic Resonance) Environment."[6]

If you would like to market stents of various sizes and shapes, then we recommend you follow our recommendations in the FDA guidance, "Assessment of Radiofrequency-Induced Heating in the Magnetic Resonance (MR) Environment for Multi-Configuration Passive Medical Devices."[7]

G. Non-Clinical Bench Testing

Some of the performance tests described in this section should be performed for all biliary stents and SDSes, whereas others should only be performed for those with specific designs (e.g., balloon expandable stents). This information is provided for each test described in this section. We believe that each test supports the determination of substantial equivalence of biliary stents.

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 a scientific justification describing why the test is not applicable.

We recommend you compare the results of these performance tests for your device to those obtained for the predicate device (refer to **Appendix A**). For information on the recommended content and format of test reports for the testing described in this section, refer to FDA's draft guidance, "Recommended Content and Format of Complete Test Reports for Non-Clinical Bench Performance Testing in Premarket Submissions."[8]

[6] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm107708.pdf

[7] https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm452644.pdf

[8] https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM606051. When final, this guidance will represent FDA's current thinking on the recommended content and format of test reports for non-clinical bench performance testing in premarket submissions.

The following tests are recommended for biliary stents:

(1) Stent Corrosion Resistance

Significance: Stent corrosion can cause or contribute to premature stent failure. In addition, corrosion byproducts may be toxic or cause other adverse biological and tissue responses.

Recommendation: We recommend that you address the corrosion properties of your device described below. If some of these characteristics do not apply to your device, we recommend that you explain this in your application.

a. Pitting Corrosion Potential

We recommend that you characterize the corrosion potential of your as-manufactured stent according to the method (or an equivalent one) described in the currently recognized version of ASTM F2129: *Standard test method for conducting cyclic potentiodynamic polarization measurements to determine the corrosion susceptibility of small implant devices*. The test setup should meet the criteria outlined in the current version of ASTM G5: *Standard reference test method for making potentiodynamic anodic polarization measurements*. Testing should be performed after subjecting the device to simulated use testing, which includes crimping, tracking, and deployment of the device through an *in vitro* fixture that mimics *in vivo* anatomic conditions. Alternatively, the stent may be subjected to strains expected during simulated use (e.g., bending) without passing through a tracking fixture, with justification. This device conditioning is intended to simulate the clinical conditions of the stent at the time of implantation. Simulated bile should be used as the standard test solution.

Test reports for pitting corrosion potential testing should be consistent with the currently recognized version of ASTM F2129. For example, test reports should include corrosion/rest potentials, breakdown potentials, description of observed corrosion with photographic documentation, as well as polarization curves. When practical, we recommend that you plot all polarization curves in one graph. You should report whether your test setup met the criteria outlined in the current version of ASTM G5. Results should be assessed against your acceptance criteria. The acceptance criteria for the pitting corrosion testing should be determined by comparison to a legally marketed predicate device. Alternatively, while there is a lack of data directly linking *in vitro* corrosion testing to *in vivo* corrosion outcomes, conservative guidelines have been published by Rosenbloom and Corbett, which may also be used to establish acceptance criteria.[9]

Literature or previous performance data may support the pitting susceptibility assessment of your stent. However, the materials, design, and fabrication processes specific to your stent may reduce or eliminate the applicability of literature or previous experience with your device. For example, the pitting corrosion resistance of nitinol is sensitive to processing variables such as heat

[9] Rosenbloom, S. N. and R. A. Corbett (2006). An Assessment of ASTM F 2129 Test Results Comparing Nitinol to Other Implant Alloys. Proceedings of the International Conference on Shape Memory and Superelastic Technologies (ASM International), Pacific Grove, CA.

treatment and surface finish, and therefore literature would not be applicable. In cases where manufacturing changes that could impact surface finish are implemented, the currently recognized version of ASTM F2129 testing or surface characterization should be performed to demonstrate that the surface is not adversely altered.

b. Galvanic Corrosion

If your stent contains more than one type of metal, such as a base stent material with added marker bands, we recommend that you demonstrate the design's resistance to galvanic corrosion. If you expect that your stents will be overlapped during clinical procedures, and the contacting or overlapping stents may be made of different materials, we recommend that you address the potential for galvanic corrosion between stents. In this case, we recommend that you use the marketed stent with the highest galvanic coupling with your stent material in your evaluation. We recommend the methods described in ASTM F3044: *Standard test method for evaluating the potential for galvanic corrosion for medical implants* or their equivalents.

As an alternative to using marketed stents for galvanic corrosion testing, coupons representing an expected worst-case galvanic coupling, that are subjected to identical manufacturing processes may be used. In addition, a justification may be provided, in lieu of testing, if the expected worst-case galvanic coupling potentials are small and if the relative surface ratios of the cathodic to anodic materials are low (e.g., marker band to stent surface ratio).

Testing should be conducted even if an alloy conforms to a specific standard because manufacturing processes can affect the galvanic corrosion potential of the finished product.

(2) Stent Dimensional and Functional Attributes

a. Dimensional Verification

Significance: Accurate stent dimensions help the physician to achieve proper stent sizing and accurate placement in the body. They also affect the functional behavior of the stent.

Recommendation: FDA recommends that you provide the information described below that applies to your stent.

Un-expanded Stents

You should provide dimensional measurements and tolerances for un-expanded stents on the deployment catheter. The results should support the dimensions in the device description.

Balloon Expandable Stents

You should measure and report the expanded diameter of balloon expandable stents. You may do this when creating a compliance chart (see **Section V.G.3.d** for recommended methods for creating a compliance chart).

Self-Expanding Stents

You should verify the unconstrained expanded diameter of self-expanding stents with measurement data.

b. Foreshortening

Significance: Foreshortening, i.e., dimensional changes to the stent that may occur during deployment, influences final stent length. Knowledge of the foreshortening characteristics aids in proper stent length selection and proper placement in the body. Foreshortening is a measurement of the difference in length between the unexpanded and expanded stent.

Recommendation: FDA recommends that you report the decrease in length of the stent between the catheter-loaded condition (unexpanded stent) and the deployed condition (expanded stent) for every length and diameter combination.

We recommend that you report the results in terms of a percentage of the loaded length as shown below:

$$\text{Percent Foreshortening} = 100 \times (\text{Change in Length} \div \text{Loaded Length}).$$

See **Section V.I below** for recommendations on data presentation of the percent foreshortening of self-expanding stents in your labeling.

c. Recoil for Balloon Expandable Stents

Significance: The recoil behavior of balloon expandable stents influences proper device selection, sizing, and acute post-implant results. Recoil is a function of stent design and material selection; therefore, knowledge of stent recoil helps to characterize the behavior of a particular stent design.

Recommendation: We recommend that you report the measured change in diameter of your stent between post-balloon expansion and after balloon deflation.

We recommend that you measure and report values for each labeled stent diameter. If you expect that the percent recoil varies significantly with length, we recommend that you evaluate different stent lengths at various points along the length of the stent, including the ends. The number of locations along the length of the stent at which recoil is measured should be determined by initial assessment of the stent geometry.

We recommend that you present the results as a percentage of the expanded diameter.

We recommend the methods described in the currently recognized version of ASTM F2079: *Standard test method for measuring intrinsic elastic recoil of balloon-expandable stents* or their equivalents.

d. Stent Integrity

Significance: Stent defects, whether a result of manufacturing flaws or subsequent damage, can contribute to clinical complications. Laser cutting or other manufacturing processes may induce flaws that are not completely removed by polishing. Plastic deformation during loading or balloon expansion may cause cracks or other damage.

Recommendation: We recommend that you examine your deployed stent and report any evidence of stent defects such as, but not limited to, the following:

- cracks;
- scratches;
- permanent set; and
- fretting.

If you expect that your stents will be overlapped during clinical procedures and the design allows for micromotion between components, such as woven wires, that may disrupt an associated coating or passive film after implantation, then we recommend that you address the possibility of fretting as part of the stent integrity testing. If applicable, overlapped stents should be subjected to physiologically relevant clinical use conditions.

Examination should be performed after subjecting the device to simulated use testing, which includes crimping, tracking, and deployment of the device through an *in vitro* fixture that mimics *in vivo* anatomic conditions. Alternatively, the stent may be subjected to strains expected during simulated use (e.g., bending) without passing through a tracking fixture, with justification. This device conditioning is intended to simulate the clinical conditions of the stent.

We recommend that you use either optical or electron microscopy, or both, to look for defects. We recommend that you support the level of magnification that you use on the basis of the size of the defect that your inspection attempts to detect.

When you are looking for damage, we recommend that you examine or inspect the following:

- for balloon expandable stents, after expansion to the largest diameter listed in your labeling; and
- for self-expanding stents, after expansion to the unconstrained diameter.

e. Radial Compression Force

Significance: Radial compression force characterizes the ability of the stent to resist collapse under external loads.

Recommendation: We recommend that you report a value for the force required to compress the stent once it is expanded.

FDA recommends that you measure and report values for each labeled stent diameter. We also recommend that you evaluate different stent lengths, including the minimum and maximum values for the smallest and largest diameters.

f. Radial Outward Force

Significance: Radial outward force is the force applied to tissues surrounding a self-expanding stent after deployment. Excessive radial outward force could injure the surrounding bile duct tissue, while a radial outward force that is too low can result in incomplete apposition of the stent to the tumor or lumen.

Recommendation: We recommend that you measure the radial outward force exerted by self-expanding stents against the contacting tissue after deployment. If a particular stent size or model is indicated for use in a range of lumen sizes, your assessment should cover the range of possible lumen sizes, or should include a rationale for not assessing the entire indicated size range. We also recommend that you evaluate different stent lengths, including the minimum and maximum values for the smallest and largest diameter stents. In addition, if you expect that the radial outward force of your stent is not axially uniform (e.g., if your stent has a tapered length or flared portions), we recommend that you measure the radial force at multiple locations along the length of the stent.

g. Radiopacity

Significance: Stent visibility using fluoroscopic or radiographic imaging generally assures proper stent placement and allows follow-up and secondary treatment.

Recommendation: FDA recommends that you evaluate the radiopacity of your stent at the smallest diameter and the shortest length during the following stages in the life of the stent:

- delivery;
- deployment, if separate from delivery; and
- post-implantation.

We recommend that you provide a qualitative or quantitative assessment 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.

(3) Stent Delivery System (SDS) Dimensional and Functional Attributes

Unless otherwise noted, we recommend that you conduct all testing on complete sterilized assemblies with mounted stents. We also recommend that you thermally equilibrate all test samples in a 37 °C saline bath.

a. Delivery, Deployment, and Retraction

Significance: The SDS should safely and reliably deliver the biliary stent to the intended location according to the instructions for use, without damage to the stent or injury to the patient. This testing is used to validate the accuracy and repeatability of the delivery system.

Recommendation: FDA recommends that you test that the SDS can safely and reliably deliver the stent to the intended location. We also recommend that you demonstrate that the stent is not adversely affected by the SDS, both during deployment and withdrawal in a relevant test model. The test model you choose should mimic actual clinical simulation parameters of the biliary anatomy including the following attributes:

- lubricity;
- tortuosity;
- stricture size; and
- length of delivery system outside the body (model).

SDS performance testing should include, but may not be limited to the following:

- tracking force;
- deployment force;
- withdrawal force; and
- deployment accuracy.

b. Balloon Rated Burst Pressure (Balloon Expandable Stents Only)

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 survive at the RBP could result in an adverse clinical outcome.

Recommendation: We recommend that you test balloons with mounted stents that are not constrained by any test fixture, such as tubing. We recommend that you conduct testing on the longest length of every stent diameter, plus the smallest diameter at the shortest length and the

largest diameter at the shortest length. **Table 2** illustrates the recommended test matrix for a stent design that ranges in diameter from 8.0 to 14.0 mm and ranges in length from 40 to 80 mm.

Table 2: Recommended Test Matrix for RBP

Stent Diameter (mm)	**Stent Length (mm)**			
	40	**50**	**60**	**80**
8.0	X			X
10.0				X
12.0				X
14.0	X			X

We recommend that you test according to the example in **Table 2** for each balloon size with a different labeled RBP. We recommend that you increase balloon pressure in uniform increments until failure.

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

- integrity of the balloon, such as a rupture or leak; and
- 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.

c. Balloon Fatigue (Balloon Expandable Stents Only)

Significance: Balloons on SDSes are often inflated multiple times during clinical use. Failure of the balloon to withstand multiple inflations could lead to adverse clinical consequences.

Recommendation: FDA recommends that you determine the repeatability, to ten inflations, of successful balloon inflation to the RBP. If you propose to market stents of various sizes, then we recommend you sample and test stents using the four corners paradigm as shown in **Table 3:**

- smallest diameter, shortest length;
- smallest diameter, longest length;
- largest diameter, shortest length; and
- largest diameter, longest length.

Table 3: Four Corners Test Paradigm Example

Stent Diameter (mm)	Stent Length (mm) 40	50	60	80
8.0	X			X
10.0				
12.0				
14.0	X			X

We recommend that you test balloons with mounted stents that are not constrained by any test fixture, such as tubing, and that you inflate the balloons in increments 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 ten 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 95% confidence.

d. Stent Diameter vs. Balloon Pressure (Compliance Chart: Balloon Expandable Stents Only)

Significance: The diameter of a deployed balloon expandable stent varies with the applied balloon pressure. A compliance chart in the labeling that relates stent diameter to balloon pressure guides selection of stent size to fit the target stricture.

Recommendation: FDA recommends that you test all stent diameters at their longest lengths. **Table 4** illustrates the recommended test matrix for a stent design that ranges in diameter from 8.0 to 14.0 mm and ranges in length from 40 to 80 mm.

Table 4: Recommended Test Matrix for Compliance Chart

Stent Diameter (mm)	Stent Length (mm) 40	50	60	80
8.0				X
10.0				X
12.0				X
14.0				X

We recommend that you identify the nominal inflation pressure and RBP, as shown in the example below. We recommend that you test multiple product lots. We also recommend that you clearly document any data rounding. **Table 5** shows a sample compliance chart for a stent with 8 mm, 10 mm, and 12 mm diameters, with a RBP of 14.0 atmospheres (atm). The nominal diameter occurs at 12.0 atm.

Table 5: Sample Compliance Chart for a Balloon Expandable Stent

Pressure (atm)	Stent Nominal Diameter where x = stent inner diameter at the given pressure		
	8.0 mm Stent Inner Diameter (mm)	10.0 mm Stent Inner Diameter (mm)	12.0 mm Stent Inner Diameter (mm)
9.0	X	x	x
10.0	X	x	x
11.0	X	x	x
12.0	8.0	10.0	12.0
13.0	X	x	x
14.0*	X	x	x

*RBP

e. SDS Bond Strength

Significance: Failure of bonds in the SDS could lead to device failure and clinical complications.

Recommendation: We recommend that you test the bond strength at locations where adhesives, thermal fusion, or other joining methods are used for bonding components of the SDS. We recommend that you precondition (e.g., track the device through simulated anatomy) the device prior to conducting this testing to ensure that SDS bond strength is maintained after tracking.

f. Crossing Profile

Significance: Changes in the cross-sectional shape and size of the SDS along its length affect the SDS's ability to cross strictures.

Recommendation: FDA recommends that you measure and report the crossing profile of your SDS, defined as the maximum distance between 2 points on the perimeter of a cross-section through the SDS. The crossing profile should be reported for the portion of the SDS between the proximal end of the mounted stent and the distal tip of the SDS. Testing should address potential differences in crossing profile that may exist in the circumferential direction (i.e., the cross-sectional shape may not be a circle). To address this issue, we recommend that you evaluate the crossing profile of your delivery system along different longitudinal paths (e.g., rotating test sample 90 degrees for measurements).

g. Balloon Inflation and Deflation Time (Balloon Expandable Stents Only)

Significance: Balloons occlude the target lumen and obstruct the flow of bile while inflated. Inflation and deflation times affect obstruction time. Inflation of a balloon for extended periods of time could lead to adverse clinical consequences.

Recommendation: FDA recommends that you specify the balloon's inflation and deflation times and demonstrate that the balloon inflates and deflates within those times. We recommend that

you describe any observed difficulties with balloon deflation or SDS extraction after deploying the stent.

h. Stent Securement for Unsheathed Stents

Significance: Dislodgment of the stent prior to deployment can result in perforation or other trauma in the target lumen. Stents without sheaths may dislodge if they catch on tortuous anatomy, guide catheters, or other devices.

Recommendation: FDA recommends that you evaluate the force that will dislodge the stent from the SDS under clinically relevant conditions. We recommend that the test include insertion through a tortuous path that simulates the anatomy of commonly stented areas of the biliary tract to and including the stricture site. We recommend that the tortuous path be sized appropriately for the stent size being tested. We recommend that you submit a photograph, diagram, or description of the tortuous path, including dimensions. We recommend that the stent sizes tested represent the worst-case stent securement for your design. We recommend that you explain why your results are applicable to all sizes of your stent, including those not tested for stent securement.

FDA recommends that you address the modes of dislodgement as described below:

Dislodgement by Forward Motion

Advancing a stent delivery system across a tight tumor could result in stent dislodgement. We recommend testing the stent by passing it through a simulated tight tumor in the tortuous path.

Dislodgement by Reverse Motion

Withdrawing a SDS through another device, such as an endoscope or guiding catheter, could result in stent dislodgement. We recommend testing the stent by attempting to withdraw the un-deployed stent into a guide catheter or other opening of the smallest size recommended in the instructions for use.

H. Clinical Performance Testing

Significance: In some cases, pre-clinical evaluation does not fully characterize all clinical experience, outcomes, and risks. In such cases, we recommend that you conduct *in vivo* (i.e., clinical) studies to evaluate device safety and effectiveness for new and modified biliary stents and SDSes.

Recommendation: Clinical evidence is generally unnecessary for biliary stents; however, such testing may be requested in situations such as the following:

- polymer covered designs;
- indications for use dissimilar from legally marketed devices of the same type that would not constitute a new intended use;

- designs or sizes dissimilar from designs previously cleared under a premarket notification;

- different technology from that used in legally marketed devices of the same type, yet does not raise different question of safety or effectiveness; and

- stents that are intended to be removable.

We will consider alternatives to clinical testing when the proposed alternatives are supported by an adequate scientific rationale. If a clinical study is needed to demonstrate substantial equivalence (i.e., conducted prior to obtaining 510(k) clearance of the device), the study should generally be conducted under the Investigational Device Exemptions (IDE) regulation, 21 CFR 812. Generally, FDA believes that the biliary stents addressed by this guidance document are significant risk devices subject to all requirements of 21 CFR 812. See the FDA Guidance titled, "Significant Risk and Nonsignificant Risk Medical Device Studies."[10] In addition to the requirements of Section 21 CFR 812, sponsors of such trials must comply with the regulations governing institutional review boards (21 CFR 56) and informed consent (21 CFR 50).

I. Labeling

The premarket notification must include proposed labeling in sufficient detail to satisfy the requirements of 21 CFR 807.87(e). Proposed labels and labeling, sufficient to describe the biliary stent and SDS, their intended use, and the directions for use must be provided.

As prescription devices, biliary stent systems are exempt from having adequate directions for lay use required under section 502(f)(1) of the FD&C Act (21 U.S.C. § 352(f)(1))) as long as the conditions in 21 CFR 801.109 are met. For instance, labeling must include adequate information for the intended user of the device, including indications, effects, routes, methods, frequency and duration of administration and any relevant hazards, contraindications, side effects, and precautions (21 CFR 801.109(d)).

The labeling for biliary stent systems should include the following information.

(1) Display of Common Name and Trade Name

As discussed in Section II, FDA has placed limitations on most biliary stent substantial equivalence determinations pursuant to section 513(i)(1)(E) of the FD&C Act. Under these limitations, FDA has required a statement in labeling that provides appropriate information regarding an intended use of the device not identified in the proposed labeling. Specifically, FDA has required the prominent display of "biliary" in close proximity to the trade name and everywhere that the trade name appears in the labeling, such as all layers of packaging (e.g., pouches, boxes, carton labels), the instructions for use, and other such materials. We recommend that the word "biliary" or "biliary stent" should be **at least** three-fourths the size of your trade

[10] https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm126418.pdf

name and using the same font style as the trade name (e.g., both displayed in Times New Roman, bold type).

(2) Device Description

We recommend that your device description include the following information:

- photographs and/or drawings that illustrate design, function, and compatibility of stent, delivery system, and all accessories;
- statement of whether the stent is balloon-expandable or self-expanding;
- list of all materials used to manufacture the stent;
- table that displays all stent diameters and lengths (when more than one model);
- description of any ancillary or accessory devices that are packaged with your stent system when no separate labeling is available;
- compatibility with guiding catheter sizes;
- balloon rated burst pressure (balloon expandable stents only); and
- specification for SDS crossing profile.

(3) Contraindications

We recommend that you include contraindications to the use of the device. Contraindications describe situations in which the device should not be used because the risk of use clearly outweighs any possible benefit.

(4) Warnings

We recommend that you include an appropriate warning if there is reasonable evidence of an association of a serious hazard with the use of the device. A causal relationship need not have been proved. For example, if your performance testing does not address having your stents overlap within the bile duct, and you intend for stents to potentially be overlapped, then we recommend you include the following warning: "The safety and effectiveness of overlapping stenting devices within the biliary tree has not been established."

A warning is also appropriate when the device is commonly used for a disease or condition for which there is a lack of valid scientific evidence of effectiveness for that disease or condition and use of the device is associated with a serious risk or hazard. As discussed in Section II, FDA has placed limitations on most substantial equivalence determinations for biliary stents pursuant to section 513(i)(1)(E) of the FD&C Act. Under these limitations, FDA has required the following statement in the Warnings section of biliary stent device labels:

The safety and effectiveness of this device for use in the vascular system has not been established.

As described in FDA's guidance, "Deciding When to Submit a 510(k) for a Change to an Existing Device,"[11] manufacturers are permitted to make certain labeling changes without submission of a new 510(k). The labeling limitations included in the "SE letter with Limitations," however, are required by section 513(i)(1)(E) of the FD&C Act. Therefore, a new 510(k) must be submitted before these limitations are modified in any way or removed from the device's labeling. Additional information regarding "SE with limitations" can be found in FDA's guidance, "Determination of Intended Use for 510(k) Devices; Guidance for CDRH Staff (Updated to K98-1)."[12] If the identical device for which clearance is being sought has also been approved for a vascular indication through a separate marketing application, this limitation may not apply.

(5) Precautions

You should include as precautions information regarding any special care physicians or others should exercise for the safe and effective use of the device. Additionally, you should include any limitations on the use of a device for reasons including, but not limited to, the following:

- lack of long-term safety and effectiveness data;
- lack of safety and effectiveness data for special patient populations;
- need for appropriate physician training; and
- anatomical or physiological limitations on the effectiveness of the device.

Stent handling, stent placement, stent system removal, and any post-implant precautions are also appropriate for inclusion in this section.

(6) MRI Safety Information

We recommend you follow the labeling guidance in "Establishing Safety and Compatibility of Passive Implants in the Magnetic Resonance (MR) Environment."[13] We also recommend that you use the standardized terminology and icons specified in ASTM F2503*: Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment*.

[11] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm514771.pdf

[12] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm082166.pdf

[13] https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm107708.pdf

(7) Overview of Clinical Studies

As we explained in **Section V.H**, clinical studies are not necessary to support many biliary stent applications. However, if clinical data is included in the submission, you should provide a narrative description of the study or studies relevant to the stent. The narrative should be brief, and for each study, it should include the following:

- description of the design of the study, including any randomization, blinding, and the control or controls used;
- statement of the number of patients enrolled;
- statement of the number of investigational sites both inside the United States (US) and outside the United States (OUS);
- description of the primary study endpoint or endpoints;
- description of the results of the study (e.g., adverse events, endpoint data, statistical analysis); and
- statement of the amount of available follow-up.

(8) Potential Adverse Events

You should include potential adverse events associated with stenting of the biliary duct, and if applicable, with endoscopic procedures.

(9) Directions for Use

You should include directions for proper preparation and use of the device. If multiple SDSes are available, you should clearly indicate differences specific to each SDS. An example would be to indicate the difference between an endoscopic and a percutaneous delivery system and to provide specific directions for each one.

Compliance Chart (Balloon Expandable Stents Only)

You should include a graphical and/or tabular presentation of inflation pressure vs. stent inner diameter (ID), i.e., a compliance chart, over the full range of recommended deployed stent diameters derived from bench testing. If you round the data, you should footnote the chart to indicate that the data is rounded. We recommend the format presented in **Table 5**.

Percent Foreshortening (Self-Expanding Stents Only)

You should provide a table that includes the following:

- stent length;

- stent diameter;
- stent length in undeployed mounted condition; and
- stent percent foreshortening defined as 100% × (undeployed length – fully expanded length)/undeployed length.

(10) Patient Labeling

You should provide examples of all patient labeling, including the patient guide and implant card, that you intend to provide to patients. When preparing patient labeling, we recommend you use the FDA guidance, "Guidance on Medical Device Patient Labeling."[14]

For MR Conditional stents, we recommend you include all conditions for safe MR use as specified in "Establishing Safety and Compatibility of Passive Implants in the Magnetic Resonance (MR) Environment,"[15] as well as the MR Conditional icon from the currently recognized version of ASTM F2503.

[14] https://www.fda.gov/downloads/medicaldvices/deviceregulationandguidance/guidancedocuments/ucm070801.pdf

[15] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm107708.pdf

Appendix A: Example Test Summary Table

See below for an example of how test summary information may be organized.

Test		Sizes Tested and Sample Sizes	Test Method or Standard Reference	Accept/Reject Criteria	Results
Material Characterization	*Material Composition				
	*Corrosion Resistance				
Stent Dimensional and Functional Attributes	*Dimensional Verification				
	*Foreshortening				
	*Recoil for Balloon Expandable Stents				
	Stent Integrity				
	*Radial Compression Force				
	*Radial Outward Force				
	MR Safety and Compatibility: a. Magnetically Induced Deflection Force b. Magnetically Induced Torque c. RF induced Heating d. Image Artifact				
	Radiopacity				
	*Delivery, Deployment, and Retraction				

Test		Sizes Tested and Sample Sizes	Test Method or Standard Reference	Accept/Reject Criteria	Results
Delivery System Dimensional and Functional Attributes	Balloon Rated Burst Pressure (*balloon expandable stents only*)				
	Balloon Fatigue (*balloon expandable stents only*)				
	Stent Diameter vs. Balloon Pressure (Compliance Chart) (*balloon expandable stents only*)				
	*Catheter Bond Strength				
	Crossing Profile				
	*Balloon Inflation and Deflation Time (*balloon expandable stents only*)				
	*Stent Securement for Unsheathed Stents				
Biocompatibility	Biocompatibility				

*Items should have results compared to those of the predicate