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Coronary, Peripheral, and Neurovascular Guidewires – Performance Tests and Recommended Labeling

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Guidance for Industry and Food and Drug Administration Staff

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This guidance supersedes "Coronary and Cerebrovascular Guidewire Guidance" issued January 1995.



U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

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Preface

Public Comment

You may submit electronic comments and suggestions at any time for Agency consideration to https://www.regulations.gov. Submit written comments to the Dockets Management Staff, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852. Identify all comments with the docket number FDA-2018-D-1775. Comments may not be acted upon by the Agency until the document is next revised or updated.

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Coronary, Peripheral, and Neurovascular Guidewires - Performance Tests and Recommended Labeling

Guidance for Industry and Food and Drug Administration Staff

This guidance represents 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 or Office responsible for this guidance as listed on the title page.

I. Introduction

This guidance document provides recommendations for premarket notification (510(k)) submissions for guidewires intended for use in the coronary vasculature, peripheral vasculature, and neurovasculature. The recommendations reflect current review practices and are intended to promote consistency and facilitate efficient review of these submissions. For the purposes of this guidance, the coronary vasculature includes blood vessels within the heart, including the ostium of the left main coronary artery; the neurovasculature includes blood vessels within the cranium, typically considered the vasculature distal to the cervical segment of the internal carotid artery; the peripheral vasculature includes all other cardiovascular vasculature. This document is intended to assist industry in designing and executing appropriate performance testing to support a 510(k) submission and provides recommendations for content and labeling to include in the submission.

For the current edition of the FDA-recognized standards 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 "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices."[1]

[1] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/appropriate-use-voluntary-consensus-standards-premarket-submissions-medical-devices

FDA's guidance documents, including this 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

Guidewires are used to facilitate the placement of therapeutic devices during percutaneous interventional procedures. In the context of this guidance, the guidewires being discussed are intended for use in the coronary vasculature, peripheral vasculature, and neurovasculature. There have been many technological advancements since the initial regulation of these devices. Therefore, updated information and additional clarity is needed regarding FDA's recommendations for performance testing and labeling for a 510(k) submission for new or modified guidewires.

This document supplements other FDA documents regarding the specific content requirements and recommendations of a 510(k) submission. You should also refer to 21 CFR 807.87 and FDA's guidance, "Format for Traditional and Abbreviated 510(k)s."[2]

III. Scope

The scope of this document is limited to guidewires indicated for use in the coronary vasculature, peripheral vasculature, and neurovasculature, regulated under 21 CFR 870.1330 and with product codes listed in the table below.

Product Code	Regulation Number	Name
DQX	21 CFR 870.1330	Wire, Guide, Catheter, Cardiovascular (Coronary and Peripheral)
MOF	21 CFR 870.1330	Guide, Wire, Catheter, Neurovasculature

IV. Premarket Submission Recommendations

A. Device Description

We recommend that you identify your device by the applicable regulation and product code described in Section III above and include the information described below.

[2] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/format-traditional-and-abbreviated-510ks-guidance-industry-and-fda-staff

- **Device components**: FDA recommends that you identify and explain the function of all components and accessories, including packaging. You should include a clear description of the basic operation of the device and identify any unique features (e.g. steerable tip), when applicable. You should also identify all sizes, configurations and models included within the scope of the submission. If your device contains any joints (i.e., locations where adhesives, thermal fusion, or other joining methods are used for bonding components of the guidewire), we recommend that you identify the joint location and bonding method used.

- **Engineering drawing(s) of the device**: FDA recommends that you provide engineering drawing(s) with all dimensions, tolerances, and components clearly labeled (e.g., tip configuration, tip performance, and dynamic material interactions (e.g., mechanism to control tip deflection)). In addition to the engineering drawing(s), a photograph of the device can also be provided. FDA recommends that you include this for each device, accessory, and/or component included within the scope of the submission.

- **Technological characteristics**: FDA recommends that you describe the technical and performance specifications and include a brief description of the device design in the device description section of the submission. 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.

- **Materials**: FDA recommends that each material(s) be clearly identified along with its corresponding contact duration. We recommend identifying both the generic material(s) of construction and the unique material identifier(s). If your device includes coating(s), we recommend that you identify the coating name, chemical formulation, coating purpose, whether the coating is hydrophobic or hydrophilic, thickness, length, location and details of how the coating is applied to the guidewire substrate. 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) for this information.

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 (21 U.S.C. 360c(i); 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 below for an example of how this information may be organized. This table is not intended to represent an exhaustive list of comparative parameters; ensure you provide all relevant device descriptive characteristics, as outlined in Section IV.A. Device Description, above.

Description	Subject Device	Predicate Device (Kxxxxxx)
Indications for Use		
Intended Use		
Wire Diameter		
Device Length		
Tip Length		
Tip Type and Shape		
Tip Flexibility		
Wire Material		
Coating(s) Material, Length and Location		
Tip Material		
Accessories		
Packaging Configuration		
Sterilization Method		
Shelf Life		

As part of your comparison, we recommend that you clearly explain the intended clinical environment and intended use of your device. The indications for use statement should identify whether the device is intended to navigate into the coronary vasculature, peripheral vasculature, and/or neurovasculature. If your device contains any feature(s) that is unique to your device compared to the predicate, we recommend that you clearly describe the feature(s), the location(s), and the operational characteristics and provide an explanation as to why the differences do not raise different questions of safety and effectiveness.

C. Biocompatibility

Significance: Guidewires contain patient-contacting materials, which, when used as intended (i.e., limited direct contact with circulating blood), may induce a harmful biological response.

Recommendation: You should determine the biocompatibility of all patient-contacting materials present in your device. If your device is identical in composition and processing methods to guidewires with a history of successful use, you may reference previous testing experience or the literature, if appropriate. For some device materials, it may be appropriate to provide a reference to either a recognized consensus standard, or to a LOA for a device 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'"[3] which identifies the types of biocompatibility assessments that should be considered and recommendations regarding how to conduct related tests.

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, guidewires are externally communicating devices with limited (<24 hour) duration direct contact with the circulating blood. Therefore, the following endpoints should be addressed in your biocompatibility evaluation:

- cytotoxicity;
- sensitization;
- irritation/intracutaneous reactivity;
- acute systemic toxicity;
- material-mediated pyrogenicity;
- complement activation (SC5b-9 pathway is recommended and C3a pathway optional);
- *in vivo* thrombogenicity; and
- direct and indirect hemolysis.

The following additional considerations are recommended for guidewires. If novel materials are used, then genotoxicity testing may also be needed. Testing should be conducted with the largest surface area device model and worst-case exposure. Test samples should represent the final, sterilized device.

D. Sterility

Significance: Depending on the intended use, guidewires will contact blood and possibly cerebrospinal fluid and therefore should be adequately sterilized to minimize infections and related complications.

Recommendation: For guidewires labeled as sterile, we recommend that you provide information for the final, sterilized device in accordance with FDA's guidance "Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile."[4]

E. Pyrogenicity

Significance: Pyrogenicity testing is used to help protect patients from the risk of febrile reaction due to gram-negative bacterial endotoxins and/or chemicals that can leach from a medical device (e.g., material-mediated pyrogens).

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[3] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-international-standard-iso-10993-1-biological-evaluation-medical-devices-part-1-evaluation-and

[4] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/submission-and-review-sterility-information-premarket-notification-510k-submissions-devices-labeled

Recommendation: To address the risks associated with the presence of bacterial endotoxins, guidewires should meet pyrogen limit specifications by following the recommendations outlined in FDA's guidance "Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile."[5] You should also follow the recommendations in "Guidance for Industry Pyrogen and Endotoxins Testing: Questions and Answers."[6] To address the risks associated with material-mediated endotoxins, follow the recommendations in FDA's guidance "Use of International Standard ISO-10993, 'Biological Evaluation of Medical Devices Part 1: Evaluation and Testing'."[7]

For devices intended to be labeled as "non-pyrogenic," we recommend that both the bacterial endotoxin and rabbit material-mediated pyrogen testing be conducted.

F. 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 testing, 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 the critical device properties to ensure 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 IV.G. Non-Clinical Performance Testing 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

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[5] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/submission-and-review-sterility-information-premarket-notification-510k-submissions-devices-labeled

[6] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-pyrogen-and-endotoxins-testing-questions-and-answers

[7] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-international-standard-iso-10993-1-biological-evaluation-medical-devices-part-1-evaluation-and

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 used to attain the expiration date. For devices or components containing polymeric materials or coatings, you should conduct testing on real-time aged samples to confirm the results of the accelerated aging study(ies). This testing can 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).

G. Non-Clinical Bench Testing

The purpose of the non-clinical bench testing is to ensure that the device performs as intended under the specified conditions of use and supports a demonstration of substantial equivalence to the predicate device. The non-clinical performance testing recommended for each device's intended use may vary based on its respective risk profile associated with the intended target vasculature. FDA recommends that you provide the information below to evaluate the material and performance characteristics of your final, sterilized device that represents the worst-case design for each performance test. Where appropriate, the performance of the proposed device should be compared to that of the predicate device.[8] If a test listed in Section IV.G. Non-Clinical Performance Testing is excluded from your submission, we recommend that you provide a clinical and risk-based justification for its omission.

For information on recommended content and format of test reports for the testing described in this section, refer to FDA's guidance, "Recommended Content and Format Non-Clinical Bench Performance Testing Information in Premarket Submissions."[9]

1. Pre-Conditioning

Pre-conditioning can include a variety of test sample preparations and may depend on the test being conducted. Prior to conducting the non-clinical performance testing, we recommend that you prepare the device per the instructions for use. For certain device characteristics being evaluated (e.g., coating integrity, particulate generation), you should also subject the device to additional pre-conditioning (e.g., extended soaking in physiologically relevant solution at 37˚C), and tracking through a simulated use model as discussed in Section IV.G.2. Simulated Use Model) to present worst-case clinical use. We recommend that you clinically justify pre-conditioning parameters used for each test, where applicable.

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[8] See FDA Guidance, "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)] - Guidance for Industry and Food and Drug Administration Staff" (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/510k-program-evaluating-substantial-equivalence-premarket-notifications-510k), for more information on comparing to a primary predicate or reference device.

[9] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/recommended-content-and-format-non-clinical-bench-performance-testing-information-premarket

2. Simulated Use Model

The simulated use model may be used when pre-conditioning or when testing in simulated anatomy is recommended. Your anatomical model should be appropriately tortuous to represent a challenging vasculature for the patient population intended to be treated. When designing your anatomical model, you should consider lumen diameter, bend radii, bend reversals, number of bends, tracking length, and coefficient of friction of tracking materials (e.g., polyurethane, silicone, Teflon, glass latex, native vessel). We recommend that your anatomical model include all relevant pathway attributes to represent the human anatomy. Should a two-dimensional anatomical model be chosen rather than a three-dimensional model, all native pathway attributes should be maintained and represented within the model. Furthermore, the anatomical model should appropriately model the various anticipated curvatures and disease states, if applicable, the device will encounter from all proposed access sites. While there are currently no standardized models of the coronary vasculature, peripheral vasculature and/or neurovasculature, an example of a tracking fixture that FDA has previously accepted in premarket submissions is described in Figure X2.4 of ASTM F2394-07: *Standard Guide for Measuring Securement of Balloon Expandable Vascular Stent Mounted on Delivery System*.

When describing your simulated use model(s), we recommend that you identify the materials of construction of the model and include images and engineering diagrams with dimensions (e.g., lengths, tubing diameters, radii of bend). We also recommend that a clinical rationale supporting the selection of the anatomical model parameters include a review of available imaging data or literature regarding the anatomy of the intended population. In addition, for devices intended to be used in the neurovasculature, your simulated use model should be as tortuous as the relevant vasculature included in your instructions for use. Specifically, we recommend that you use a full three-dimensional anatomical model including the intended access site (e.g., femoral, radial) to the intended target location in the neurovasculature. To simulate a clinically challenging tortuosity, your full neurovascular anatomical model should include, at a minimum, the Internal Carotid Artery (ICA) siphon, two (2) 180-degree turns and two (2) 360-degree turns, at the distal portion of the anatomical model. Alternative neurovasculature anatomical models should be justified with respect to clinically challenging neurovasculature tortuosity based on the intended use of the device and/or specific performance test being evaluated.

3. Dimensional Verification

Significance: Accurate device dimensions help the physician to select appropriate product sizes. They can also affect the functional behavior of the device.

Recommendation: We recommend providing dimensional specifications and tolerances for the device as manufactured. The tolerances chosen should be based on risk and should have an appropriate clinically or scientifically relevant justification. We recommend using a calibrated tool to verify each dimension. At a minimum, the length and outer diameter should be measured and reported. If applicable, tip length, coating length, or other guidewire features should also be reported.

4. Visual Inspection

Significance: Guidewire defects, including kinks, cracks, deformations or debris, can contribute to clinical complications, affecting the safety and performance of the device.

Recommendation: We recommend testing to ensure that the devices are free of extraneous matter and surface defects due to processing that could cause trauma to the vessels during use. If the device is coated, the coating should appear uniform. We recommend examining the devices with a minimum 2.5X magnification. This test may be conducted independently or in conjunction with another performance test if performed prior to performance testing to represent the as-manufactured product. Please note that for coated devices, visual inspection alone at 2.5X magnification is likely insufficient to adequately evaluate the coating integrity and additional test considerations should be followed (see Section IV.G.10. Coating Integrity).

5. Simulated Use

Significance: Use of the device in a simulated use model, in combination with other interventional devices, as appropriate, can provide more clinically relevant information about its performance than isolated bench top performance testing.

Recommendation: We recommend that you use your device in combination with ancillary devices (e.g., introducer, guiding catheter) according to the instructions for use and track the device through the simulated use model multiple times. Please see Section IV.G.2 Simulated Use Model for recommendations in developing your anatomical model. You should report observations regarding compatibility with ancillary devices, appropriate preparation, and the maneuverability of the device through the simulated use model. You should also report the integrity of the device prior to, during (e.g., kinking, compromised push ability), and after use. This test may be conducted in conjunction with other tests when appropriately justified.

6. Tensile Strength

Significance: Joint failure could lead to device failure and/or vessel damage.

Recommendation: We recommend testing the strength of each unique joint to failure. If there are multiple joints composed of the same material and adhesion method, then the worst-case joint may be used to represent all joints. Prior to testing we recommend that the samples are prepared per the instructions for use and then pre-conditioned as needed to simulate worst-case conditions and tracked through a simulated use model. Tensile strength testing should demonstrate that your device is capable of withstanding tensile forces greater than those expected in clinical use. When setting your acceptance criteria, we recommend that you consider testing the predicate device concurrently or determine the theoretical force based on clinical information. When the acceptance criteria are established, a clinical basis for their appropriateness should be included in your protocol. Because the strain rate used may affect the resulting data, and thus, the acceptability of the acceptance criteria and results, we also recommend that you report the strain rate used to test each sample and justify this rate.

7. Tip Pull

Significance: Tip detachment may adversely impact clinical performance (e.g., result in distal embolization).

Recommendation: For guidewires that contain one or more joints at the distal tip (e.g., spring or coil tips), we recommend evaluating the tensile force to separate the distal tip from the guidewire. Prior to testing, we recommend that the samples are prepared per the instructions for use and then pre-conditioned as needed to simulate worst-case conditions and tracked through a simulated use model. This test may be performed as part of the tensile strength assessment (see Section IV.G.6 Tensile Strength above), if applicable.

8. Torque Strength

Significance: Inability to withstand torsional forces typical of clinical use (i.e., torqueing/rotating the device to navigate to the target vasculature) may lead to device failure and/or vessel damage.

Recommendation: We recommend that you prepare the samples per the instructions for use, pre-condition as needed to simulate worst-case conditions and track each device through a simulated use model. We recommend the distal end of the device be constrained from movement and the proximal end of the guidewire be rotated until failure. We recommend that you report the number of rotations to failure and the failure mode for each device tested.

9. Torqueability

Significance: An inability of the distal tip to respond to manipulations made at the proximal end may adversely impact clinical performance (e.g., whipping effects may cause vessel damage and/or inability to navigate vessels).

Recommendation: We recommend that you prepare the samples per the instructions for use, pre-condition as needed to simulate worst-case conditions and track each device through a simulated use model. With the sample in the simulated use model and the distal end unconstrained, we recommend that you rotate the proximal end of the guidewire. You should report the rotational input to the resulting distal rotation at 90-degree intervals (with your applied rotation angle determined with reference to the device risk and intended use) and calculate a proximal-to-distal rotational ratio for each sample.

10. Coating Integrity

Significance: Coating separation (i.e., peeling, flaking, shedding delamination and/or sloughing off) or degradation may adversely impact clinical performance (e.g., result in inflammation at access site, pulmonary embolization, pulmonary infarct, myocardial embolization, myocardial infarct, embolic stroke, cerebral infarct, tissue necrosis, or death).[10]

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[10] See FDA Safety Communication on "Lubricious Coating Separation from Intravascular Medical Devices", at http://wayback.archive-it.org/7993/20170722215712/https://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm473794.htm.

Recommendation: Coating integrity testing should include an interpretation of the data collected (including a discussion of why any observed defects are acceptable given the intended use and potential risk associated with the intended use) before and after subjecting the device to simulated use testing in a representative tortuous model. We recommend assessing the device for any coating delamination or degradation during simulated use. You should provide representative images (using scanning electron microscopy and/or optical microscopy) of the coated surface pre- and post-simulated use testing. Images should be taken using ≥40X magnifications in order to detail any coating defect. Multiple magnifications (up to 500X) may be needed to properly visualize any observed defects. If your coating is clear, it may be beneficial to dye the coating prior to assessing the device surface in order to allow for proper visualization. It may be helpful to include baseline (i.e., before simulated use) reference samples for comparative purposes if the guidewire is dyed. We recommend that you conduct the coating integrity testing simultaneously with the particulate evaluation as described in Section IV.G.11. Particulate Evaluation to assess the origin, quantity, and size of particulates that may be removed from your device during simulated use. If your device contains coating defects, you should provide a scientific rationale explaining why the coating anomalies do not pose a safety risk.

11. Particulate Evaluation

Significance: Particulate generation during clinical use may result in serious adverse events including pulmonary embolism, pulmonary infarction, myocardial embolism, myocardial infarction, embolic stroke, tissue necrosis and death; therefore, guidewires intended to navigate the coronary vasculature or neurovasculature pose the greatest clinical risk and should be evaluated for particle generation along with coating integrity assessment in a representative simulated use model. If your device is intended to only navigate the peripheral vasculature and the coating integrity evaluation identified coating defects (e.g., along the length of the guidewire) that may raise additional clinical concerns, particulate evaluation may be needed to address potential safety concerns.

Recommendation: To accurately account for particulates generated during the use of your device, the particles should be characterized after simulated use. We recommend that the number of particulates generated at each evaluation be quantified and characterized by size and count using a validated method (e.g., light obscuration, light refraction) under continuous flow conditions to simulate blood flow. Specifically, we recommend that the total number of particulates be reported in the following size ranges: ≥ 10µm, ≥ 25µm, and at the largest size for which validation yields ≥ 75% recovery. At a minimum, the largest size should be ≥ 50µm. For particulates that are greater than 50 µm, we recommend that you distinguish, by percentage, the amount that are ≥ 200 µm, ≥ 500 µm and ≥ 1000 µm, if those measurement methods are available, as these larger sized particulates pose a greater embolic risk.

Appropriate precautions should also be implemented to ensure that the particles are suspended during particle counting and sizing to minimize aggregation and other artifacts from the test system. For further guidance on particulate evaluation, please refer to Section VIII.A.13. of FDA Guidance for Industry and FDA Staff, "Class II Special Controls Guidance Document for Certain Percutaneous Transluminal Coronary Angioplasty (PTCA) Catheters" (https://www.fda.gov/regulatory-information/search-fda-guidance-

documents/class-ii-special-controls-guidance-document-certain-percutaneous-transluminal-coronary-angioplasty).

You should provide a clinical discussion explaining why the results of the particulate evaluation and the associated coating integrity assessments do not raise a safety concern. If the particulate evaluation raises safety concerns, then chemical characterization may be needed to identify the particulate source(s).

12. Lubricityy

Significance: Lubricious coatings may be incorporated to decrease frictional forces experienced when navigating the target vasculature, and the functionality and performance of these coatings should be demonstrated.

Recommendation: We recommend that you characterize the drag force of the coating (e.g., pinch test) after the samples are prepared per the instructions for use and then pre-conditioned as needed to simulate worst-case conditions. In addition to coating integrity testing (Section IV.G.10), you should consider assessing the coating durability by performing the lubricity test multiple times (i.e., a clinically relevant number of passes). The mechanism of lubrication (e.g., hydrodynamic) should be identified. Any observations (e.g. the changes in the drag forces with cycling, coating defects using high resolution imaging) and conclusions should be reported.

13. Corrosion Resistance

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

Recommendation: We recommend that any metallic component of the device be examined for signs of corrosion after an immersion test (e.g., exposure of the device to a series of saline baths at room temperature, boiling, and 37˚C beyond the maximum expected clinical use duration). For more information regarding recommendations of methodology for this testing, please refer to the currently recognized version of ISO 10555-1: *Intravascular catheters – Sterile and single-use catheters – Part 1: General requirements, Annex A*. Although this standard has been written for intravascular catheters, the method used to evaluate corrosion resistance is applicable to guidewires.

14. Kink Resistance

Significance: Guidewires may be subjected to bending forces during use, and an inability to withstand forces that are typical of clinical use could lead to device failure and/or vessel damage.

Recommendation: Your device should demonstrate resistance to kinking (and other failure modes) when bent around anatomically relevant radii. The samples should be prepared per the instructions for use and then pre-conditioned as needed to simulate worst-case conditions. To evaluate the resistance to kinking, you should bend the guidewire around mandrels of

decreasing radii until kink, plastic deformation, and/or fracture occurs or to the smallest bend radii expected during clinical use, whichever comes first. This evaluation should account for all joints. When reporting the results, you should identify the mandrel sizes tested, which mandrel caused device failure, the location of failure and the type of failure observed.

15. Tip Flexibility

Significance: Safe and successful navigation through tortuous vessels relies on the mechanical properties of the guidewire tip. Inappropriately designed guidewire tips may result in vessel perforation, dissection and/or other vessel damage.

Recommendation: After the samples are prepared per the instructions for use and then pre-conditioned as needed to simulate worst-case conditions, we recommend that you identify the force that induces buckling deformation when the device is held at 5, 10 and 20 mm from the distal tip.

16. Radiopacity

Significance: Insufficient radiopacity could impede safe and appropriate usage of the device as it will not be clearly visible during use.

Recommendation: We recommend choosing a sample size up to 5 devices to ensure that the radiopaque markers or radiopaque portions of the device are visible using clinical imaging techniques. We recommend a qualitative or quantitative measure of radiopacity, wherein the guidewire is compared to a standard material or predicate device as a control via real-time or plain film x-ray. It is acceptable to use data acquired as part of animal studies, *in vitro* phantoms, or equivalent models.[11] For additional information regarding recommendations of methodology for this testing, please refer to the currently recognized version of ASTM F640: *Standard Test Method for Determining Radiopacity for Medical Use*. We recommend including high-quality images of the guidewires and the control(s) in your submission.

A. 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 guidewires.

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

- indications for use in complex clinical scenarios (e.g., crossing chronic total occlusions (CTOs)) of the coronary and peripheral arteries;

[11] FDA supports the principles of the "3Rs," to reduce, refine, and replace animal use in testing when feasible. We encourage sponsors to consult with us if they wish to use a non-animal testing method they believe is suitable, adequate, validated, and feasible. We will consider if such an alternative method could be assessed for equivalency to an animal test method.

- cases where engineering and/or animal testing raise issues that warrant further evaluation with clinical evidence;
- indications for use dissimilar from legally marketed devices of the same type; or
- new technology, i.e., technology different from that used in legally marketed devices of the same type yet does not raise different questions of safety or effectiveness.

We will consider alternatives to clinical testing (such as animal 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 must be conducted under the Investigational Device Exemptions (IDE) regulation, 21 CFR Part 812. Generally, FDA believes guidewires 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."[12] 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 Part 56) and informed consent (21 CFR Part 50).

In some cases, "real-world data" (RWD) may be used to support expansion of the indication for a device for which 510(k) clearance has already been obtained. Whether the collection of RWD for a legally-marketed device requires an IDE depends on the particular facts of the situation. Specifically, if a cleared device is being used in the normal course of medical practice, an IDE would likely not be required. For additional information regarding this topic, please refer to the FDA Guidance entitled "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices."[13]

B. 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 guidewires, their intended use, and the directions for use must be provided.

As a prescription device, guidewires are exempt from having adequate directions for lay use required under section 502(f)(1) of the Federal Food, Drug and Cosmetic Act (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)).

For additional recommendations regarding coated devices, please see FDA's guidance "Labeling Considerations for Intravascular Catheters, Wires, and Delivery Systems with

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[12] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/significant-risk-and-nonsignificant-risk-medical-device-studies

[13] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-real-world-evidence-support-regulatory-decision-making-medical-devices

Lubricious Coating"[14], which includes specific labeling recommendations for this subset of guidewires. The instructions for use or package insert should include the following information. The list below is not intended to be exhaustive of all the labeling requirements under part 801.

1. Device Description

We recommend that you include a description of the guidewire identifying the important components and the functions of each such as the length, outer diameter along the length including transition zones, tip shape, coating location(s) and characteristics (e.g., hydrophobic or hydrophilic), if applicable.

2. Indications for Use Statement

The indications for use statement described in the labeling should be supported by information in the 510(k) submission and clearly identify any specific regions of the vasculature.

3. Contraindications

We recommend including contraindications to describe situations in which there are known hazards or risks, as applicable, in the instructions for use. If you believe there are no known contraindications, please state "none known".

4. Warnings/Precautions

We recommend including the following warnings/precautions, as applicable, in the instructions for use. Sample language is provided in italics. If you believe any of these warnings/precautions are not applicable to your device, please provide a justification for each omission.

- A warning statement regarding the indications for which the device has been confirmed to perform as intended, such as the following: "*The safety and effectiveness of the device has not been established or is unknown in vascular regions other than those specifically indicated.*" For example, if a specific guidewire is only indicated for peripheral vascular use based on the information provided in the 510(k) submission, the device should include a warning that the safety and effectiveness of the device has not been established in the coronary vasculature or neurovasculature.
- A warning against reuse or re-sterilization of the device, which could affect medical device materials and components, such as "*This device is intended for single use. Do not reuse or re-sterilize.*"
- A warning statement about the unestablished safety and effectiveness of a reprocessed device intended for multiple uses. For example, *"The device is intended for single-patient use and should not be reprocessed or used after reprocessing."*

[14] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/intravascular-catheters-wires-and-delivery-systems-lubricious-coatings-labeling-considerations

- Guidewires should be used under fluoroscopic guidance. We recommend that you consider the inclusion of important precautions and/or warnings to ensure the safety of device use associated with fluoroscopy for both patients and clinical operators.

5. Potential Adverse Events

We recommend that you include information on the potential adverse events that may result from use of your device. FDA acknowledges that the specific adverse events may depend on the specific design and intended use of the device. Such adverse event may include, but are not limited to:

- Access site complications
- Allergic reaction (to contrast, device or other)
- Aneurysm
- Angina or unstable angina
- Bleeding/hemorrhage
- Cardiac tamponade/pericardial effusion
- Death
- Embolization (plaque, thrombus, device, tissue, or other)
- Infection
- Myocardial infarction or ischemia
- Stroke/cerebral vascular accident (CVA)/transient ischemic attack (TIA)
- Thrombosis/Thrombus
- Vasospasm
- Vessel trauma, perforation, dissection
- X-Ray radiation exposure complications (e.g., alopecia, burns ranging in severity from skin reddening to ulcers, cataracts, and delayed neoplasia)

6. Directions for Use

We recommend that you provide specific directions for use of the guidewire. If your device contains a coating(s), then the directions for use should clearly explain how to properly prepare the device prior to clinical use.

V. Modifications

In accordance with 21 CFR 807.81(a)(3), a device modification "that could significantly affect the safety or effectiveness of the device" or represents "a major change or modification in the intended use of the device" requires a new 510(k). The changes or modifications listed below would likely require submission of a new 510(k). Note that this list is not exhaustive but provides examples of modifications that will generally require submission of a new 510(k). For additional details, please see FDA guidance "Deciding When to Submit a 510(k) for a Change to an Existing Device."[15]

Such changes or modifications include:

[15] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-change-existing-device

- Guidewire Material – A change in core guidewire material could significantly affect both safety and effectiveness of the device by altering the biocompatibility risk profile or device performance.
- Coating(s) Location, Material, Amount, or Processing – A change in the coating composition, location, and the processes used to apply the coating could significantly affect both safety and effectiveness of the device by altering the biocompatibility risk profile and/or device performance.
- Dimensions Not Previously Cleared – A change to a critical dimensional characteristic of the guidewire that is beyond the previously cleared range for your device could significantly affect both safety and effectiveness by significantly affecting the performance risk profile.
- Tip Configuration – A change to the tip shape, material, or adhesion process could significantly affect both the safety and effectiveness of the device because of a change to the known risk of tip detachment and the ability of the guidewire to properly navigate the intended vasculature.
- Additional Vasculature – A change in the target vasculature could significantly affect both safety and effectiveness due to new or altered risks associated with different clinical conditions than those previously addressed in prior submissions.

FDA believes that the following changes or modifications would likely not require submission of a new 510(k):

- minor changes to the device packaging (e.g., hard copy of the Instructions for Use is replaced by an electronically available copy);
- an extension of shelf life implemented according to the test protocols previously reviewed under the cleared submission; or
- a dimensional change within the existing specification tolerance or a critical dimensional characteristic that is within the range of the previously cleared device.