Peripheral Vascular Atherectomy Devices - Premarket Notification [510(k)] Submissions

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.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draft document within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance.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 should with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this document, please contact the Peripheral Interventional Devices Branch at 301-796-2520.

FDA U.S. FOOD & DRUG ADMINISTRATION
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U.S. Department of Health and Human Services
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Preface

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Peripheral Vascular Atherectomy Devices - 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Draft Guidance for Industry and Food and Drug Administration Staff

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic.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 or Office responsible for this guidance as listed on the title page.

I. Introduction

This draft guidance document provides recommendations for 510(k) submissions for peripheral vascular atherectomy device. This draft guidance is issued for comment purposes only.

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, "Recognition and Use of Consensus Standards".[1]

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.

[1] https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm077295.pdf

II. Background

Atherectomy is an interventional procedure performed to debulk atherosclerotic plaque from diseased arteries. Atherectomy has been used in treatment of both coronary and peripheral arterial disease. The mechanism of plaque removal ranges from cutting, shaving, sanding or vaporizing.[2,3] Atherectomy devices vary in design and complexity and there are currently four main categories of atherectomy devices:[4,5]

1. Directional: Directional atherectomy involves the resection of atherosclerotic plaque with a cutting device in the longitudinal plane. Directional atherectomy typically removes plaque in a single plane with multiple passes.

2. Rotational: Rotational atherectomy devices typically employ a high-speed concentrically rotating cutting blade coated with abrasive material. These devices utilize differential and circumferential cutting blades to debulk plaque.

3. Orbital: Although similar to rotational atherectomy devices, orbital atherectomy devices employ a 360° rotational coil with a rough burr that "sands" off plaque. The orbital motion allows the burr to remove plaque as it moves through the lesion. Unlike rotational atherectomy, the orbit of this type of atherectomy device changes with rotational speed.

4. Laser: Laser atherectomy systems use a high-energy light beam to vaporize plaque. The device typically consists of a fiber-optic catheter that attaches to a laser generator.

The choice of atherectomy device depends on plaque location, vessel characteristics, length of disease segment, plaque quantity, plaque texture, and physician experience.

We encourage members of industry to engage CDRH via the Pre-Submission process to obtain feedback based on your device indications and operational characteristics. For more information on Pre-Submissions, please see the FDA guidance, "Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff"[6]; hereinafter, Pre-Submission Guidance).

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[2] Mustapha, Jihad A. "Atherectomy Today: Go Slow to Finish Fast." *Endovascular Today*, October 2011, pp. 56-66.
[3] Akkus, Nuri I., Abdulrahman Abdulbaki, Enrique Jimenez, and Neeraj Tandon. "Atherectomy Devices: Technology Update." *Medical Devices: Evidence and Research*, vol. 8, 2015, pp. 1-10.
[4] Ibid.
[5] Quevedo, Henry C., Salman A. Arain, Gholam Ali, and Nidal Abi Rafeh. "A Critical View of the Peripheral Atherectomy Data in the Treatment of Infrainguinal Arterial Disease." *Journal of Invasive Cardiology*, vol. 26, no. 1, 2014, pp. 22-29.
[6] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm311176.pdf

Atherectomy devices used in the peripheral vasculature require a premarket notification [510(k)] submission before marketing (see 21 CFR part 807). This document supplements other FDA documents regarding the specific content requirements and recommendations of a premarket notification (510(k)). You should also refer to 21 CFR 807.87 and FDA's guidance, "Format for Traditional and Abbreviated 510(k)s."[7]

III. Scope

The scope of this document is limited to atherectomy devices used in the peripheral vasculature, regulated under 21 CFR 870.4875 and with product code listed in the table below:

Product Code	Regulation Number	Name
MCW	870.4875	Intraluminal Artery Stripper

Due to the higher-risk anatomical location, atherectomy devices used in the coronary vasculature are class III devices, which require a premarket approval (PMA) application before marketing. (see sections 513(a)(1)(C) and 515 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 360c(a)(1)(C) and 360e) and 21 CFR part 814). Atherectomy devices indicated for use in the coronary vasculature are outside the scope of this guidance document; however, some of the information provided in this guidance document may be applicable to atherectomy devices with coronary indications. For more information on FDA's recommendations for review of coronary atherectomy devices, please contact the Interventional Cardiology Devices Branch (ICDB).

A new atherectomy device might not fall neatly into the four categories listed above; however, the information provided in this guidance may still be helpful in developing a risk analysis and performance testing strategy. Please note that other devices used to facilitate passage of a guidewire through or around chronic total occlusions or devices used for plaque modification, but do not intentionally remove plaque (e.g., cutting/scoring devices), are not within the scope of this document. However, some testing strategies in this guidance document may also be helpful for evaluating these device types.

IV. Premarket Submission Recommendations

A. Device Description

We recommend that you identify your device by regulation and product code as described in Section III above and include the information describe below. As part of the device description, we also recommend that you identify all components and accessories and describe their

[7] https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm084365.htm

function(s). In addition, we recommend that you provide the following information, if applicable to your device:

- description of the mechanism of operation;
- description of technological characteristics;
- identification of configurations and models;
- listing of materials;
- identification of coatings; and
- images or engineering drawings.

We recommend that you describe the technical and performance specifications of the device and include a brief description of the device design in this section. The specifications may include measurement tolerances, operating limitations (e.g., rotation speed, energy output, wavelength, orbital lumen diameter) and any other functional, physical, and environmental specifications of the device. We also recommend that you describe ranges and/or accuracy of the specifications. If your submission includes multiple device models, we recommend that you identify all device models and configurations. You should also provide images or engineering drawings of the device and accessories that include dimensions and tolerances to fully describe and characterize the device and describe any unique device features.

Also, as part of your device description, we recommend that you provide a list of all device components, their respective materials, and their contact duration. We recommend identifying both the generic material(s) of construction and the unique material identifier(s). You should also provide the level of blood contact (i.e., direct, indirect, or no contact) for each component.

B. Predicate Device 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); and 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 should provide all relevant device descriptive characteristics as outlined in the "Device Description" section, above.

Table 1: **Predicate Device Comparison.**

Description	Subject Device	Predicate Device (Kxxxxxx)
Indications for Use		
Mechanism of Operation		

Description	Subject Device	Predicate Device (Kxxxxxx)
Material		
Measurement Tolerances		
Rotation Speed		
Energy Wavelength		
Orbital Lumen Diameter		
Other Relevant Characteristics		

As part of your comparison, we recommend that you clearly explain the intended clinical environment and intended use of the device, including target vasculature.

C. Software

Significance: Software in atherectomy devices ensures that malfunctions that could be hazardous do not occur (e.g., cause injury, erroneous diagnosis or delay in delivery). Adequate software performance testing provides assurance that the device is safe for the user, operator and the patient.

Recommendation: Refer to the FDA software guidance, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices"[8] for a discussion of the software documentation that you should provide in your submission. The software guidance outlines the type of documentation to be provided based on the "level of concern" (LOC) associated with the device. We generally consider the software for atherectomy devices to present a moderate LOC. However, new or unusual indications, applications, or technological characteristics may result in a higher level of concern. If you believe that the software in your device presents either a "minor" or a "moderate" level of concern as defined in the software guidance, you should provide a scientific justification that supports your rationale of the level of concern based on the possible consequences of software failure.

We recommend that you provide a full description of the software/firmware supporting the operation of the subject device in accordance with the Software Guidance, commensurate with the appropriate level of concern. This recommendation applies to original device/systems as well as to any software/firmware changes made to already-marketed devices. Changes to software must be revalidated and reverified in accordance with Design Controls (21 CFR 820.30(g)(i)) and documented in the Design History File (21 CFR 820.30(j)). Some software changes may warrant the submission of a new 510(k). For further information on this topic, please refer to "Deciding When to Submit a 510(k) for a Software Change to an Existing Device."[9]

[8] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm089593.pdf
[9] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm514737.pdf

As appropriate, you should also provide information on the Cybersecurity aspects of your device. For more information on this topic, please see the FDA guidance, "Content of Premarket Submissions for Management of Cybersecurity in Medical Devices."[10]

If the device includes off-the-shelf software, you should provide the additional information as recommended in the FDA guidances, "Off-the-Shelf Software Use in Medical Devices"[11] and "Cybersecurity for Networked Medical Devices Containing Off-The-Shelf (OTS) Software"[12], which provide additional information regarding medical devices utilizing off-the-shelf software.

Overall, the documentation related to the software contained in the medical device should provide sufficient evidence to describe the role of the software included in the device and performance testing to demonstrate that the software functions as designed.

D. Biocompatibility

Significance: Peripheral vascular atherectomy devices contain patient-contacting materials, which, when used for their intended purpose, 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 atherectomy devices 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 reference a recognized consensus standard or provide 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 and manufacturing (including sterilization and packaging) 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, discuss 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 the FDA guidance, "Use of International Standard ISO-10993-1, 'Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk

[10] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm356190.pdf

[11] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm073779.pdf

[12] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm077823.pdf

management process'"[13], 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,, atherectomy devices are external-communicating devices in contact with circulating blood for a limited contact duration. Therefore, the following endpoints should be addressed in your biocompatibility evaluation:

- cytotoxicity;
- sensitization;
- irritation or intracutaneous reactivity;
- acute systemic toxicity;
- material mediated pyrogenicity; and
- hemocompatibility.

Please note that genotoxicity testing may be requested if the atherectomy device contains novel patient-contacting materials that have not been previously evaluated for use in contact with circulating blood in legally marketed medical devices.

The following additional considerations are recommended regarding sample preparation for atherectomy devices. For biocompatibility testing conducted using extraction samples, we recommend the following:

- Determine the appropriate amount of test material, as outlined in *ISO-10993-12: Biological evaluation of medical devices – Part 12: Sample preparation and reference materials* or an equivalent method, using surface area to extractant volume ratios (mass to extractant volume ratios should only be used if surface area cannot be calculated).
- Use both polar and nonpolar extractants, where applicable.
- Explain any changes in the post-extraction vehicle (compared to pre-extraction), including color, presence of any particles, etc.
- Describe the details of storage conditions (e.g., storage time, temperature), if applicable.

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

E. Sterility

Significance: Peripheral vascular atherectomy devices come in contact with blood and should be adequately sterilized to minimize infections and related complications.

Recommendation: For atherectomy devices labeled as sterile, we recommend that you provide information for the final, sterilized device in accordance with the FDA guidance, "Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile."[14]

F. 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).

Recommendation: To address the risks associated with the presence of bacterial endotoxins, atherectomy devices should meet pyrogen limit specifications by following the recommendations outlined in the FDA guidance, "Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile."[15]. You should also follow the recommendations in "Guidance for Industry Pyrogen and Endotoxins Testing: Questions and Answers."[16] To address the risks associated with material-mediated endotoxins follow the recommendations in FDA's guidance "Use of International Standard ISO-10993-1, 'Biological Evaluation of Medical Devices Part 1: Evaluation and Testing' ."[17]

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

G. 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

[14] https://www.fda.gov/downloads/medicaldevices/deviceregulationsandguidance/guidancedocuments/ucm109897.pdf

[15] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm109897.pdf

[16] https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm310098.pdf

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

description of the package integrity test methods and a summary of the results, 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 critical device properties to ensure that it will perform adequately and consistently during the entire proposed shelf life. To evaluate device functionality, we recommend you assess each of the bench tests described in Section IV.I and IV.J 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 subjected to accelerated aging, we recommend that you specify the way in which the devices were aged. We recommend that you age your devices per ASTM F1980: *Standard guide for accelerated aging of sterile barrier systems for medical devices* and specify the environmental parameters established to attain the expiration age. 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).

H. Electrical Safety and Electromagnetic Compatibility (EMC)

Significance: Most atherectomy devices are medical electrical equipment and therefore may expose the operator and patient to hazards associated with the use of electrical energy or may fail to operate properly in the presence of electromagnetic disturbance. If your atherectomy device includes a laser radiation source, laser safety conditions and standard safety considerations apply as there is a risk for ocular and skin tissue damage.

Recommendation: Peripheral vascular atherectomy devices should be tested to demonstrate that they perform as anticipated in their intended use environment. We recommend that this testing be performed as described in the currently FDA-recognized versions of the following standards for medical electrical equipment safety and electromagnetic compatibility:

- AAMI/ANSI/ES 60601-1: *Medical electrical equipment – Part 1: General requirements for basic safety and essential performance*; and

- AAMI/ANSI/IEC 60601-1-2: *Medical electrical equipment – Part 1-2: General requirements for basic safety and essential performance – Collateral standard: Electromagnetic disturbances – Requirements and tests*.

If submitting a declaration of conformity to the above standards, we recommend that appropriate supporting test data and analysis be provided because this series of standards includes general methods with multiple options and, in some cases, does not include specific acceptance criteria or address assessment of results. For additional information on providing EMC information in a premarket submission, please see the FDA guidance, "Information to Support a Claim of Electromagnetic Compatibility (EMC) of Electrically-Powered Medical Devices."[18]

When a laser atherectomy device has the potential laser radiation hazards to the eyes and skin of the patient and operator, safety measures such as the use of personal protective equipment (laser protective eyewear) and/or skin contact sensors should be included to mitigate the risk.

I. Battery Testing

Significance: If your device is battery-operated, it is important to confirm that the battery is capable of performing effectively in a clinical setting. Inadequate battery operation could lengthen the time of procedure, which could impact patient safety and treatment effectiveness.

Recommendation: We recommend that you describe all batteries used in the system. Your description should include performance characteristics (e.g., usable battery amp-hour capacity, shelf-life and life testing under worst-case usage). For evaluation of battery safety and performance, we recommend providing the following:

(1) Hazard Analysis

You should include a hazard analysis as it relates to the battery and function in the system.

(2) Qualification Testing

We recommend evaluating the suitability and performance of the battery for the intended use. The tests should reflect the risks identified in the hazard analysis and should also assess the characteristics and general reliability of the battery when subjected to stresses anticipated under normal usage and worst-case condition. For qualification testing, we recommend referencing the standards listed below:

- *IEC 62133: Secondary cells and batteries containing alkaline or other non-acid electrolytes – Safety requirements for portable sealed secondary cells, and for batteries made from them, for use in portable applications*;

[18] https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM470201.pdf

- *IEC 60086-4: Primary batteries – Part 4: Safety of lithium batteries*;
- *UL 2054: Standard for household and commercial batteries*; and
- *UL 1642: Standard for lithium batteries.*

(3) Performance Testing Considerations

When conducting the qualification testing, we recommend taking the following into consideration if your device is battery-powered:

- If a battery is pre-installed in the device (e.g., in the atherectomy catheter handle), it is important to note that a battery will self-discharge, even if the device is not turned on; this could limit the shelf-life of the device. We recommend that you evaluate the device at the proposed shelf-life. Specifically, the atherectomy catheter should have an expiration date consistent with the shelf-life of the battery and the catheter's sterility.

- If a battery is part of the sterile device system, sterilization of the battery at extreme conditions (e.g., high temperatures) could affect the battery's properties and limit performance. Therefore, we recommend taking the conditions into consideration during your qualification testing.

- If a replacement battery is needed to complete a full procedure, we recommend that you ensure that replacing a worn-out battery with a new (or fully charged) battery will not compromise device sterility.

- If the battery drives a motor connected to a rotating component, we recommend ensuring that the battery and/or the motor does not overheat during long operations. We recommend that you provide information on how the risk of overheating is mitigated (e.g., vent holes in the battery housing). If the battery requires venting (e.g., if over-discharged)[19] and the battery housing includes vent holes to allow the battery to safely vent, we recommend that you provide information regarding how the risk of water ingress into the battery component is mitigated.

J. Non-Clinical Bench Testing

The design characteristics of your device will determine the appropriate non-clinical testing to be performed. The purpose of the non-clinical bench tests is to ensure that the device design achieves the intended use at baseline (time zero) and after aging to support the device shelf-life. For information on the recommended content and format of test reports for the testing described

[19] Venting is defined as the release of excessive internal pressure from a cell/battery in a manner intended by design to preclude rupture or explosion per IEC 62133, clause 3.10.

in this section, refer to FDA's Draft guidance, "Recommended Content and Format of Test Reports for Non-Clinical Bench Performance Testing in Premarket Submissions."[20]

(1) Risk Analysis

The risk profile of your device will depend upon its intended use. In your submission, we recommend that you provide a summary of your risk analysis. If you decide not to perform a particular test for evaluation of your device performance and/or safety profile, you should provide a clinical or scientific rationale based on your risk analysis.

(2) Test Sample Selection

If your device is available in more than one size or model, the device that is deemed the worst-case should be evaluated for each respective test. You should identify the worst-case size and provide a rationale on how the selected size is representative of your size range and models.

(3) Test Sample Preparation: Pre-Conditioning

As previously mentioned, testing should be conducted on the final sterilized device. Prior to and/or during bench testing, you should apply clinically relevant pre-conditioning to the device (e.g., pre-soaking in 37°C water bath and tracking through a simulated-use model). Pre-conditioning of the device should simulate the worst-case clinical and physiological conditions that the device is expected to experience.

(4) Simulated-Use Model

Significance: The simulated-use model should adequately mimic the anatomy for which the device is intended. The use of a valid simulated use model for evaluation of device functionality helps to create a better understanding of how a device is expected to perform *in vivo* in a clinical setting.

Recommendation: Functional tests and pre-conditioning should be performed using a simulated-use model. We recommend providing the following information pertaining to your simulated-use model:

- Your simulated-use model should be appropriately rigorous in order to represent the majority of the patient population intended to be treated. Considering that atherectomy devices are intended to remove plaque, we recommend incorporating simulated atherosclerotic/rigid calcified plaque in your model in consideration of the worst-case clinical scenario. In addition, you should provide a clinical/scientific rationale (i.e., based on literature or experience) for your plaque model. If the anatomical model does not

[20] https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM606051.pdf. 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.

contain simulated plaque, we recommend evaluating the ability to remove plaque in a cadaver model.

- We recommend that you utilize a three-dimensional model in order to best represent the human anatomy. Furthermore, it should appropriately model the various curvatures expected to be encountered from all the proposed access sites.

- We recommend that you include detailed engineering drawings and/or photos of your anatomical model(s), including measurements for the different lengths, tubing diameters, and radii of curvatures (in millimeters).

- You should also provide a clinical rationale to support the selection of the anatomical model parameters.

(5) Engineering Testing

The following are recommended engineering tests for evaluating substantial equivalence of peripheral vascular atherectomy devices. Note that the tests are not all-inclusive. Thus, it is important to ensure that unique attributes specific to your device are adequately evaluated for substantial equivalence. For catheter testing, we also recommend referencing FDA's "Class II Special Controls Guidance Document for Certain Percutaneous Transluminal Coronary Angioplasty (PTCA) Catheters"[21] (hereinafter, PTCA Catheters Guidance).

a. Dimensional Analysis

Significance: Accurate device dimensions are important to aid the physician in selecting the appropriate product size. The dimensions should meet the established specification for each device size.

Recommendation: We recommend that you provide dimensional specifications and tolerances for your device as manufactured. We recommend that the specified tolerances should be based on your risk analysis. In order to provide accurate and consistent measurements, we recommend the use of a calibrated tool.

The following should be evaluated for any atherectomy device:

- crossing profile;
- inner diameter;
- working length; and
- effective length;

For directional devices:

- cutter length; and
- cutter diameter;

[21] https://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm225145.htm

For rotational and orbital devices:

- rotating component length; and
- rotating component diameter.

b. Simulated-Use Testing

Significance: The device should perform safely and reliably when used as intended or according to the recommended Instructions for Use, including techniques for preparation, delivery, use, retraction, and removal. Failure to perform as expected may lead to prolonged procedure times, device damage, or patient injury.

Recommendation: The following attributes should be evaluated during simulated-use testing:

- The device should be deliverable via the intended access point (e.g., femoral access) without vascular damage.
- The device is compatible with materials and accessories expected to be used with your device (e.g., guidewire, sheath).
- The device can be appropriately prepared prior to use.
- The device is able to track smoothly through the tortuous path and lesions to verify ease of use. The device should be appropriately flexible to traverse the simulated-use model (with plaque) without kinking or damage.
- The device should be visualized with appropriate imaging guidance. You should address any device changes (e.g., defects, kinks, debris) on your device before and after testing.
- The device is able to maintain structural integrity prior to delivery, during use, and during retraction.
- If your device contains a coating, we recommend that you provide images of the coating at 2.5× magnification before and after testing. Any changes in the coating (e.g., decreased uniformity, delamination, cracks) should be addressed.
- If your device contains software, we recommend that you validate use of the software component during simulated-use testing. Please see Section C.

c. Kink Resistance

Significance: Inability to withstand torsional forces that are typical of clinical use (e.g., when the distal tip is not free to rotate) could lead to device failure or vessel damage.

Recommendation: We recommend evaluating kink resistance of the device under the worst-case radius of curvature expected during clinical use. For example, we recommend that you consider wrapping the catheter around a series of mandrels with successively smaller radii until the catheter kinks or the lumen collapses. We also recommend you provide the clinical basis for your acceptance criteria.

d. Corrosion Resistance

Significance: Corrosion of components fabricated from metal may lead to device failure or patient risk (e.g., toxicity, embolization).

Recommendation: Evaluation of the corrosion resistance of the device during worst-case clinical use should be conducted per the test sample conditioning in accordance with ISO 10555-1:2013 *Intravascular catheters – Sterile and single-use catheters – Part 1: General requirements, Annex A.*

e. Heat Generation

Significance: Rotation of the device can cause heat generation due to friction between device parts and between the rotating tip and tissues (especially if there are rigid calcified areas). Similarly, energy from the laser can also generate heat. Increased heat may lead to tissue injury or necrosis.

Recommendation: We recommend evaluating the maximum temperature rise of your device during simulated use. A clinical and/or scientific rationale for the acceptance criteria should be supported by literature (i.e., why increase in temperature within a specific range will not impart tissue damage). If you have multiple device sizes, you should evaluate the worst-case model. For example, the largest tip at the fastest recommended rotation is expected to generate the most heat for rotational atherectomy devices.

f. Torsional Strength

Significance: Inability to withstand torsional forces that are typical of clinical use (e.g., when the distal tip is not free to rotate) could lead to device failure or vessel damage.

Recommendation: We recommend that you measure the torque strength of the atherectomy device when the distal tip is not free to rotate by rotating the proximal end of the catheter until failure. We recommend that you pre-condition the atherectomy system prior to evaluating torque strength by tracking through a tortuous path fixture, as described in Section IV.J(4). We recommend that you report the number of rotations to failure and the failure mode for each sample tested. Additionally, we recommend that you test the delivery system in a fixture that simulates worst-case expected anatomy. We also recommend you provide the clinical basis for your acceptance criteria.

g. Tensile Strength

Significance: Failure of bonds in the catheter could lead to device failure, vessel damage, and/or embolic risk due to device remnants within the vasculature.

Recommendation: We recommend evaluating the tensile force of all the joints on your device after pre-conditioning (i.e., tracking through a simulated-use model in a water bath

at 37°C). We recommend providing an image with all the joints labeled. If you choose to reference standards (e.g., *ISO 10555-1: Intravascular catheters – Sterile and single-use catheters – Part 1: General requirements*) for establishing your test method, we still recommend inclusion of a clinical and/or scientific rationale to support your acceptance criteria for your device in the intended anatomy.

h. Rotational Speed

Significance: Inappropriate or non-stable rotational speed could lead to device failure or vessel damage.

Recommendation: We recommend evaluating the rotational speed specified in your labeling and the speed stability over the proposed treatment time. It is beneficial to include the rotational speed of the predicate device for comparison. If the rotational speed is higher than that of the predicate and other FDA-cleared atherectomy devices, a discussion should be included to confirm that the proposed speed is not a safety concern. This speed should be supported with an animal study and/or clinical data (i.e., clinical study or cadavers).

i. Tip Robustness

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

Recommendation: We recommend evaluating the integrity of your catheter tip under the expected clinical conditions. Your device tip should be able to withstand constant impact on plaque under the expected number of clinical cycles. If your device tip also serves as a flushing tool, the number of tissue removal cycles the tip can withstand should be determined.

j. Plaque Removal Efficiency

Significance: Inadequate plaque removal may lead to increased procedural time. This test is intended to characterize the debulking capability under simulated conditions.

Recommendation: We recommend characterizing the plaque removal efficiency in terms of percentage of plaque removed, luminal gain, or mass of tissue removed per pass. This test can be conducted either in a simulated-use model or cadaver model. For devices with multiple models or settings (e.g., speeds), we recommend evaluating the plaque removal efficiency at the minimum and maximum specified settings.

k. Infusion Flow Rate

Significance: Inability to achieve acceptable flow rates could lead to user error, increased procedural time, device overheating, and/or tissue damage.

Recommendation: For atherectomy devices intended to infuse saline or contrast agents, the appropriate flow-rate range should be established to ensure that the flow rate is consistent and safe. Thus, we recommend validating the device flow rate and providing a rationale for why the flow rate is clinically acceptable.

l. Aspiration Rate

Significance: Inadequate aspiration rate could lead to vessel damage or build-up of debris, resulting in device failure and debris embolization.

Recommendation: If applicable, we recommend evaluating both the infusion and aspiration/suction rate and confirming that the selected rate is adequate to remove emboli but not excessive enough to cause vessel collapse or injury. This test should be conducted in a simulated-use model and supported with animal study data.

m. Debris Removal and Collection

Significance: Inadequate debris removal could lead to build-up of debris, resulting in device failure and debris embolization.

Recommendation: If applicable, we recommend evaluating the effectiveness of the removal mechanism in a diseased model (i.e., benchtop model, animal model, or cadaver model).

n. Embolization Analysis

Significance: Distal embolization is an inherent risk with treatment of peripheral artery disease with atherectomy. Migration of large emboli could result in patient injury.

Recommendation: We recommend capturing and evaluating downstream emboli content post-atherectomy and quantifying the particulates using a bench and/or animal model. Your analysis should determine whether the type, size, and quantity of emboli are clinically acceptable. If a downstream filter is used during the clinical study, the type, size, and quantity of the embolic contents present in the filter should be evaluated.)

o. Life Cycle/Fatigue

Significance: Atherectomy systems are often used multiple times. Failure of the atherectomy device to withstand multiple cycles could lead to device failure or vessel damage.

Recommendation: We recommend that you evaluate your device under the worst-case expected number of insertions and runtime. We recommend that you provide clinical rationales to support the number of insertions and runtime tested. Any changes or deformations to the atherectomy device after testing should be reported.

If your device contains an inflatable balloon that assists with cutter or tip apposition, we recommend evaluating balloon fatigue, rated burst pressure, balloon compliance, and inflation and deflation time. Please refer to the PTCA Catheters Guidance for details.

If your device has an automated handle, we recommend that you verify that device operation under user control can withstand the maximum number of cycles expected during clinical use. Please also refer to the Automated Handle Functionality Testing section below.

p. Orbit Testing

Significance: For an orbital atherectomy system, the maximum orbital diameter is dependent on plaque rigidity, diameter of the rotating component, rotational speed (rpm), and the number of passes through the lesion. Inadequate speeds may lead to device failure, increased treatment times, and/or vessel damage.

Recommendation: We recommend orbit testing at speeds specified in your labeling in a simulated-use model containing a plaque model. We also recommend that you provide a clinical/scientific rationale for your acceptance criteria and confirm that the orbits created at your pre-determined speeds are not expected to impart vessel damage.

q. Coating Integrity

Significance: Coating delamination or degradation could result in embolized particulates that could cause clinical complications.

Recommendation: If a coating is present on your device, you should provide the following:

- name of the coating;
- a description of the physical structure of the coating;
- location of the coating;
- length of the coating;
- representative images using scanning electron microscopy (SEM) and/or optical microscope of the coated surface before and after simulated-use testing at baseline (time zero) and post-aging. If your coating is clear, it may be beneficial to dye the coating prior to simulated use in order to allow for proper visualization. Please note that although standard visual inspection is typically conducted at lower magnification (≤2.5×), evaluation of coating integrity is expected to be conducted at higher magnifications in order to clearly identify and characterize any defects in the coating; and
- a summary of your results should be provided. If coating delamination or defect is observed, the coating reduction or particulates should be quantified, and a clinical rationale for why the results are clinically acceptable should be provided.

r. Automated Handle Functionality

Significance: The automated handle should function as intended. Inadequate control of the atherectomy system could lead to device failure, increased treatment time, and patient injury.

Recommendation: If your device contains an automated handle, you should evaluate its functionality as part of the bench or animal study. We recommend verifying that the distal tip orientation/torque capability operates as expected in worst-case simulated anatomy. Additionally, you should evaluate the rotational response of the atherectomy system upon activation by the automated handle and verify that the device does not rotate unexpectedly upon activation.

(6) Additional Engineering Testing for Devices Intended to Treat In-stent Restenosis

If your atherectomy device is also intended for treatment of ISR, we recommend conducting the bench tests specified below in addition to conducting a thorough risk analysis to evaluate the risks due to stent and atherectomy device interaction. If applicable, the risk assessment should include an analysis of the stent (e.g., metal exposure, stent fatigue, post-fatigue corrosion) due to interaction with the atherectomy device. If you decide to omit any of the tests specified below, we recommend providing a rationale based on your risk analysis.

a. Simulated-Use of Atherectomy Device in a Stent

Significance: Interaction with the stent could lead to device failure, stent fracture, and vessel damage.

Recommendation: We recommend evaluating the atherectomy system in an *in vitro* or *in vivo* model containing both a stent and plaque (e.g., using a diseased model or overstretch model). Visual inspection should be conducted with the naked eye and under SEM of both the stent and atherectomy device pre- and post-testing. The vessel should be assessed for damage. See Section IV.K for additional information regarding animal testing.

b. Heat Generation

Significance: High heat generation due to interaction between the atherectomy system and stent could lead to device failure and tissue damage.

Recommendation: We recommend evaluating heat generation under *in vitro* simulated-use conditions. The acceptable limit of heat generation, if any, should be supported by literature and/or clinical data.

c. Embolization Analysis

Significance: For in-stent restenosis (ISR) treatment, migration of metallic particles downstream as a result of stent and atherectomy device interaction could also result in patient injury.

Recommendation: For atherectomy devices intended for ISR treatment, the quantity, identity, and size of metallic particulates should also be evaluated. Your analysis should determine whether the type and quantity of emboli are clinically acceptable. If a downstream filter is used during the clinical study, the quantity, identity, and size of the embolic contents present in the filter should be evaluated.)

K. Animal Testing

Significance: Animal testing is generally recommended to evaluate the *in vivo* safety of peripheral vascular atherectomy devices, particularly for new designs, significant device modifications, new indications (e.g., ISR), and/or specific anatomies.

Recommendation: Animal testing of atherectomy devices should address factors that cannot be evaluated through bench tests or in a clinical study. The study design and endpoints should be based upon the mechanism of action of the device and mitigation of associated risks.

FDA supports the principles of the "3Rs," to reduce, refine, and replace animal use in testing when feasible. You should consider the best practices for the development, conduct, and presentation of these animal studies while incorporating modern animal care and use strategies. In addition, we encourage you to consult with FDA if you wish to use a non-animal testing method that you 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.

We encourage manufacturers to take advantage of the Pre-Submission Program to ensure that the animal study protocol addresses safety concerns and contains elements which are appropriate for a regulatory submission (i.e., the study should be performed under Good Laboratory Practice (GLP) regulations as stated in 21 CFR part 58 at an animal study facility with appropriate licensure and accreditations). In addition, if you are proposing to use a non-animal testing method that you believe is suitable, adequate, validated, and feasible, we recommend that you discuss the proposal using the Q-Submission Program. We will consider if such an alternative method could be assessed for equivalency to an animal test method. For details on the Q-Submission Program, please refer to the guidance "Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff."[22]

[22] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm311176.pdf

(1) Animal Model

An ideal animal model should be representative of the human atherosclerotic disease. Unfortunately, there are currently no animal models that completely mimic the human pathology.[23,24] Despite this limitation, animal models can provide safety information that cannot be obtained through other assessments. Therefore, we recommend the use of a porcine or ovine large animal model due to the similarities in cardiovascular system size and anatomy, which have demonstrated suitability for translation to humans. For details on animal study recommendations, please refer to the FDA guidance, "General Considerations for Animal Studies for Cardiovascular Devices."[25]

Although experimental animal models of atherosclerosis do exist (i.e., swine diet-induced atherosclerotic model or simulated plaque), the cost and time involved with developing the test systems with intravascular lesions often make these models prohibitive to yield robust data for regulatory safety studies. Healthy native vessel models are therefore typically employed and represent the worst-case scenario due to direct contact of the debulking portion of the device with the intima versus a hard atherosclerotic lesion, as is intended for clinical use. This factor and species-related differences are taken into consideration when interpreting the data for the premarket submission. Additional animal models may be applicable to evaluate specific intended uses or anatomies. For example, as noted above, an overstretch model may be employed to generate stenosis in a stent for evaluating atherectomy systems in ISR. [26,27]

(2) Study Endpoint Considerations

When defining your study endpoint, we recommend that animal safety studies for atherectomy devices should contain both acute and chronic testing elements that utilize the specified predicate device(s) as the control article. The elements we generally recommend evaluating in animal studies for atherectomy devices are as follows:

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[23] Kapourchali, Fatemeh Ramezani, Gangadaran Surendiran, Li Chen, Elisabeth Uitz, Babak Bahadori, and Mohammed H. Moghadasian. "Animal Models of Atherosclerosis." *World Journal of Clinical Cases*, vol. 2, no. 5, 2014, pp. 126-132.

[24] Li, Xiangdong, Yuanwu Liu, Hua Zhang, Liming Ren, Qiuyan Li, and Ning Li. "Animal Models for the Atherosclerosis Research: A Review." *Protein & Cell*, vol. 2, no. 3, 2011, pp. 189-201.

[25] https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM220772.pdf

[26] Schwartz, Robert S., Joseph G. Murphy, William D. Edwards, Allan R. Camrud, Ronald E. Vlietstra, and David R. Holmes. "Restenosis after Balloon Angioplasty. A Practical Proliferative Model in Porcine Coronary Arteries." *Circulation*, vol. 82, 1990, pp. 2190-2200.

[27] Touchard, Arturo G., and Robert S. Schwartz. "Preclinical Restenosis Models: Challenges and Successes." *Toxicologic Pathology*, vol. 34, 2006, pp. 11–18.

a. Acute Testing (Day 0)

Acute testing should capture:

- user data (as rated by qualified independent interventionalists), including:
  - ease of use/usability;
  - catheter trackability in vascular anatomy;
  - visibility on standard imaging; and
  - compatibility with accessory devices;
- major adverse events;
- acute procedural vascular safety via angiography for overall vessel integrity, including:
  - dissection;
  - filling defects;
  - stenosis;
  - thrombosis; and/or
  - other abnormalities;
  - acute procedural evaluation, including hemolysis and downstream emboli (size and type); and
- examination of device for thrombus-acute thrombogenicity.

b. Chronic Study Data (Days 28+)

Duration of testing and evaluation timepoints should be based upon mechanism of action, identified risks, expected resolution of the inflammatory response, and vascular healing. We generally recommend a 28- to 30-day observation period following treatment. However, longer studies may be warranted if healing is not observed at 30 days. In your submission, we recommend providing a justification for the chosen timepoints based upon device design and mechanism of action. If unsure, we recommend utilizing the Pre-Submission Program to obtain feedback on your study protocol; please refer to the Pre-Submission Guidance. The chronic study endpoints should include:

- major adverse events;
- in-life clinical observations;

- imaging of vascular treatment site by angiography or other imaging modalities for vascular integrity/patency, filling defects, and stenosis at baseline, interim timepoints, and at sacrifice;

- clinical pathology at baseline and at time of sacrifice;

- complete necropsy with focus on vascular treatment sites, major organ systems and downstream tissue beds for thromboembolic events;

- histopathology of vascular treatment sites for injury (external elastic lamina (EEL)/internal elastic lamina (IEL) integrity), intimal thrombi, inflammation, endothelialization, hemorrhage, and mineralization; and

- histomorphometric evaluation of vascular treatment sites for stenosis, as appropriate.

L. Clinical Performance Testing

Significance: Non-clinical evaluation does not fully characterize all relevant clinical experience, outcomes, and risks needed to demonstrate substantial equivalence. As previously noted, a diseased animal model with clinically relevant challenging anatomy and lesions does not currently exist. We believe a clinical study evaluating multiple operators, patient demographics, and lesion characteristics represents the least burdensome approach to demonstrate substantial equivalence. Therefore, we recommend that you conduct *in vivo* (i.e., clinical) studies to evaluate device safety and effectiveness for new and modified peripheral vascular atherectomy devices.

Recommendation: Clinical data are typically expected for new devices, devices modified in design and/or functionality (e.g., modification to the debulking portion of the atherectomy device), and new indications for use or labeling changes associated with device benefit or improved clinical outcomes. Due to the multivariable considerations for establishing the need for clinical data, FDA recommends having a discussion via the Q-Submission process early in device development or when modifications are proposed; please refer to the Pre-Submission Guidance.

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 Exemption (IDE) regulation, 21 CFR part 812. Generally, FDA believes that atherectomy devices addressed by this guidance are significant risk devices subject to requirements set forth in 21 CFR 812. Please see the FDA guidance, "Significant Risk and Nonsignificant Risk Medical Device Studies."[28] In addition to the requirements of 21 CFR part 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).

[28] https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126418.pdf

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 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, "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices."[29]

(1) Considerations for the Level of Clinical Evidence

The level of clinical evidence will depend on several factors, including but not limited to the following:

a. Proposed Indications for Use

If the device is intended to be used as the primary treatment (e.g., in lieu of percutaneous transluminal angioplasty (PTA)), clinical evidence should be provided to demonstrate that the device has equivalent safety and effectiveness compared to PTA or another atherectomy device with regards to meaningful clinical outcome measures (e.g., major adverse events, patency, target lesion revascularization measured at 6 months).

b. Use with Other Endovascular Therapies

If you propose to label the atherectomy device to be used in conjunction with PTA, stenting, or other endovascular therapies, the contribution of the atherectomy device should be demonstrated in a clinically meaningful way. Clinical data may be needed to support labeling of the devices when used in combination with other endovascular therapies. Your labeling should accurately reflect the outcome of your clinical study.

c. Novelty of Design

For new or modified designs and technologies, clinical data may be expected to be provided to support a substantial equivalence determination. FDA recommends that you assess the need for additional clinical testing based on your device operational characteristics via the Pre-Submission Program; please refer to the Pre-Submission Guidance.

d. Use in Specific Lesion Types

Clinical data should be provided if your device is intended to treat specific anatomies or lesion types (e.g., below-the-knee, ISR lesions, long lesions) in your indications for use or labeling. For example, patients with ISR lesions should be independently studied (e.g., separate arm, separate study) given the unique characteristics of these lesions as well as the potential for interactions between devices that may impact clinical outcomes.

[29] https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm513027.pdf

(2) Study Endpoint Considerations

We recommend that you conduct a multi-center, prospective study designed to collect data to support the safety and effectiveness of your device. As previously noted, a diseased animal model with clinically relevant challenging anatomy and lesions does not currently exist. Therefore, we believe a clinical study represents the least burdensome approach to demonstrate substantial equivalence while evaluating multiple operators, patient demographics, and lesion characteristics. The sample size should be determined based on sound clinical and statistical principles. The study endpoints and results should be compared to known outcomes for alternative atherectomy therapies. Patient selection should include both clinical and anatomical criteria (e.g., Rutherford categorization, lesion diameter/length, lesion location). We recommend considering the following safety and effectiveness evaluations:

a. Safety Assessment

For all planned studies, data regarding a composite of Major Adverse Events (MAEs) adjudicated by an independent Clinical Events Committee (CEC) should be captured. MAE may be defined as the composite of the occurrence through 30-day follow-up of all-cause death, unplanned major amputation, and target limb revascularization (TLR).

b. Performance Assessment

Demonstrating performance of an atherectomy device generally includes: (1) a measure of acute technical success (e.g., residual diameter stenosis after treatment) and (2) a measure of clinical success (e.g., target lesion revascularization at 6 months).

We may consider alternatives to clinical testing when the proposed alternatives are supported by an adequate scientific rationale. We suggest that you contact FDA to discuss clinical study planning early in your device development process.

M. 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 peripheral vascular atherectomy device, its intended use, and the directions for use, must be provided. As noted previously for specific non-clinical tests in Section IV.J, your labeling should include relevant attributes (e.g., rotational speed(s), duration of treatment, aspiration characteristics) of your device to promote its safe and effective use.

As prescription devices, peripheral vascular atherectomy devices are exempt from having adequate directions for non-prescription use under section 502(f) of the FD&C Act (21 U.S.C. 352(f)) as long as the conditions in 21 CFR 801.109 are met. For instance, labeling must include adequate information for practitioner use 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)).

V. Modifications

In accordance with 21 CFR 807.81(a)(3), a device change or 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 guidances "Deciding When to Submit a 510(k) for a Change to an Existing Device"[30] and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device."[31]

Such changes or modifications include:

- Significant change in device dimensions: FDA considers this change to be a modification in design that could alter the device performance, which in turn could impact the safety and effectiveness of the device. Thus, if dimensional changes are not in the range previously cleared, test data reports should be provided for FDA review to support the change.

- Change to the debulking component or mechanism (e.g., change from directional to orbital): FDA considers this change to be a modification in design. FDA has determined that this change could significantly affect safety and effectiveness of the device as it could change how the device operates and interacts with blood vessels. More specifically, change in the debulking component could also impact the extent of vessel trauma, which could pose a safety risk.

- Supplier or materials change to a critical component (e.g., rotation component, catheter coating): FDA considers this change to be a modification in material. FDA has determined that this change could significantly affect safety and effectiveness of the device as a change in supplier and/or materials may affect performance and/or introduce different types or quantities of residual chemicals, which could result in a toxic response, corrosion, or device failure.

- Change in the laser component specifications: FDA considers this change to be a modification in design. FDA has determined that a change in the laser component specifications (e.g., laser generator type, optical fiber density, laser modes, device crossing profile, device working length) could significantly affect safety and effectiveness of the device by potentially influencing laser output parameters (e.g., pulse duration, output energy, repetition rate), which would ultimately influence how the device effectively targets and ablates lesions. To support a change in laser component

[30] https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm514771.pdf

[31] https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM514737.pdf

specifications, new testing should be provided to demonstrate that the device does not ablate lesions outside the expected range of use such that it would pose a safety risk or affect ablation effectiveness.

- Change in sterilization technique: FDA considers this change to be a significant change. FDA has determined that this change could affect the safety and effectives of the device as it could impact device sterility and biocompatibility. For example, changes to an ethylene oxide sterilization process may leave increased ethylene oxide residuals. Additionally, changes in sterilization may unintentionally affect device materials, which could consequently affect the safety and effectiveness of the device.

- Significantly altered user technique (e.g., change from manual to automatic feature): FDA considers this change to be a significant change. FDA has determined that this change could significantly affect safety and effectiveness of the device by altering the extent of user control, which could significantly impact how the device interacts with the patient.

- Change in power source: FDA considers this change to be a modification in energy source. FDA has determined that his change could significantly affect the safety and effectiveness of the device by introducing new risks that were not previously considered or evaluated in a prior 510(k) submission. For example, a change from AC power to DC power in the form of a rechargeable battery may alter the failure modes. For example, a battery can fail due to over-charge or over-discharge, while AC power usually does not have this failure mode. Alternately, if a non-rechargeable battery is used to power the catheter, then the capacity of the battery would limit the device use-time while AC power would allow for potentially limitless device use time. Thus, it is important for FDA to evaluate changes in the power source to ensure safe and effective use of the device.

Changes or modifications in the indications for use or labeling could significantly affect both the safety and effectiveness of the device. The following changes are examples that would require a 510(k) submission.

- Change in specific lesion characteristics (e.g., ISR) or a change in specific vasculature (e.g., below the knee, upper extremities); and

- labeling changes to capture improvement of outcomes in combination with other technologies (e.g., pre-treatment with atherectomy improves outcomes of angioplasty or drug-coated balloon). This type of labeling change should be supported with bench and/or clinical data because utilization of atherectomy in combination with other therapies could impact patient safety when considering the extent or level of treatment the patient is expected to receive.

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

- Minor change in packaging: A minor change in packaging (e.g., removal of hardcopy Instructions for Use from the box and replacement with an electronic version, update to the expiration date) is not expected to impact device safety and performance.

- Increase in shelf-life: An increase in device shelf-life is not expected to impact device safety and performance as long as the testing protocols and acceptance criteria have been previously reviewed and accepted (e.g., in the original 510(k)). Additionally, the test results should fall within the acceptance criteria previously found to be acceptable.