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

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Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on July 13, 2020

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draft document within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance.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

For questions about this document, contact OHT2: Office of Cardiovascular Devices/Division C: Division of Coronary and Peripheral Interventional Devices/Plaque Modifications Team at (301) 796-2520.

When final, this guidance will update and supersede the applicable sections of "Peripheral Vascular Atherectomy Devices - Premarket Notification [510(k)] Submissions," issued on February 13, 2020.

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

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

Preface

Additional Copies

Additional copies are available from the Internet. You may also send an e-mail request to CDRH-Guidance@fda.hhs.gov to receive a copy of the guidance. Please include the document number 19047 and complete title of the guidance in the request.

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Draft Guidance for Industry and Food and Drug Administration Staff

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic.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

FDA has developed this draft guidance to propose select updates to the FDA guidance document "Peripheral Vascular Atherectomy Devices - Premarket Notification [510(k)] Submissions."[1] The existing guidance on peripheral vascular atherectomy devices remains in effect, in its current form, until this draft select update is finalized. FDA intends to incorporate this draft select update guidance with the existing guidance into one final guidance document after obtaining and considering public comment on these select updates. The proposed sections referenced below are intended to replace applicable sections of or add new section(s) to the existing atherectomy guidance after FDA considers public comment on this draft select update. FDA does not intend to substantively change the sections of the existing atherectomy guidance that are not affected by this select update.

For the current edition of the FDA-recognized standard(s) referenced in this document, see the FDA Recognized Consensus Standards Database.[2] For more information regarding use of consensus standards in regulatory submissions, please refer to the FDA guidance titled "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices."[3]

[1] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/peripheral-vascular-atherectomy-devices-premarket-notification-510k-submissions

[2] https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm.

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

II. Non-Clinical Testing Recommendations

FDA is proposing to update only a subset of the recommendations included in Section IV of the existing atherectomy guidance document.

C. Software

Significance: Software in atherectomy devices may include a variety of functions ranging from ensuring that malfunctions that could be hazardous do not occur (e.g., cause injury, erroneous diagnosis, or delay in delivery) to directly controlling device cutting/lasing output. 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"[4] 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 of atherectomy devices to present a moderate LOC. However, new or unusual indications, applications, or technological characteristics (e.g., atherectomy devices with software to control the device's cutting/lasing functions) may result in a higher level of concern. If you believe that the software in your device presents either a "minor" or a "moderate" LOC as defined in the software guidance, you should provide a scientific justification that supports your rationale of the LOC 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."[5]

[4] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-content-premarket-submissions-software-contained-medical-devices

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

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."[6]

If the device includes off-the-shelf software, you should provide the additional information as recommended in the FDA documents titled, "Off-the-Shelf Software Use in Medical Devices"[7] and "Cybersecurity for Networked Medical Devices Containing Off-The-Shelf (OTS) Software,"[8] which provide additional information regarding medical devices using off-the-shelf software.

FDA has recognized various voluntary consensus standards that support medical device interoperability which is one way to ensure appropriate functional, performance, and interface requirements of these devices. If your device has the ability to exchange and use information through an electronic interface with another medical/nonmedical product, system, or device, you should provide the additional information as recommended in the FDA guidance, "Design Considerations and Pre-market Submission Recommendations for Interoperable Medical Devices."[9]

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.

F. Pyrogenicity

Significance: Pyrogenicity testing is used to help protect patients from the risk of febrile reaction caused by gram-negative bacterial endotoxins and 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." You should also follow the recommendations in "Guidance for Industry Pyrogen and Endotoxins Testing: Questions and Answers."[10] To address the risks associated with material-mediated endotoxins, follow the

[6] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/content-premarket-submissions-management-cybersecurity-medical-devices-0
[7] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/shelf-software-use-medical-devices
[8] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cybersecurity-networked-medical-devices-containing-shelf-ots-software
[9] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/design-considerations-and-pre-market-submission-recommendations-interoperable-medical-devices
[10] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-pyrogen-and-endotoxins-testing-questions-and-answers

recommendations in FDA's guidance "Use of International Standard ISO-10993-1, 'Biological Evaluation of Medical Devices Part 1: Evaluation and Testing'."[11]

Peripheral vascular atherectomy devices should be labeled as "non-pyrogenic" as they come into contact with circulating blood. We recommend that both bacterial endotoxins and material-mediated pyrogenicity be addressed. Devices in contact with the cardiovascular system should meet pyrogen limit specifications discussed in the FDA guidance, "Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile."[12]

J. Non-Clinical Performance Testing

(5) Engineering

b. Simulated-Use Testing

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. Furthermore, 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 integrity and performance are unaffected when used in combination with applicable ancillary devices (e.g., introducer, guiding catheter, embolic protection device).
- The device is 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 before 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 (e.g., distal component, catheter shaft, cutting component) is able to maintain structural integrity prior to delivery, during use (at all labeled rotational speeds by using all mechanisms of achieving the desired rotational speed(s) and functional modes), and during retraction.
- The catheter distal component (e.g., catheter tip) can withstand constant impact on plaque under the expected number of clinical cycles as evidenced by appropriate visual

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

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

assessment. If your distal component also serves as a flushing tool, the number of tissue removal cycles the distal component can withstand should be determined. The catheter should also be evaluated for possible distal component detachment.

- 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.
- If your device contains a coating, we recommend that you provide images of sufficient magnification to fully characterize the coating coverage and potential defects. Apart from standard visual inspection (e.g., 2.5X), please also conduct coating inspection at higher magnifications (e.g., 40-500X)) to clearly identify and characterize any defects in the coating. Any changes in the coating (e.g., decreased uniformity, delamination, cracks) should be addressed. Please refer to Section **Error! Reference source not found.** for further details.
- If your device contains software, we recommend that you validate use of the software component during simulated-use testing. Please see Section C above.

l. Debris Removal and Collection

Significance: Inadequate debris removal could lead to build-up of debris, resulting in device failure and/or 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) via quantitative and qualitative methodologies.

o. 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 during your specified intended run time of the device are not expected to impart vessel damage. We also recommend that you include orbit performance data in your device instructions for use (IFU) (e.g., reference graphs depicting typical orbit diameter versus duration of operation (as measured in simulated lesions) for each device size and speed).

r. Particulate Evaluation

Significance: Particulate generation from the device during clinical use may result in serious adverse events. If your coating integrity evaluation identified coating defects that may raise additional clinical concerns, particulate evaluation may be needed to address potential safety concerns.

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Recommendation: If your device has a coating, to accurately account for particulates generated during the use of your device, the particles should be characterized and data should be interpreted after simulated use.

Test Samples

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

Test Methods

We recommend that you evaluate particulate generated by the entire atherectomy system, including accessory devices expected to be used during a clinical procedure. Catheters should be tracked through a tortuous path fixture (as described above in Sections J(4) Simulated Use Model and J(5)b Simulated-Use Testing). When delivered to the site of interest, the device should be in direct contact with the simulated vessel without the use of other coatings, lubricants, sheaths, or protective wraps between the device and the simulated vessel. To ensure measurement of the total number of particles that could be potentially introduced into the bloodstream, the catheter should be inserted into the test fixture to the extent at which it would be inserted in clinical 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.

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. We recommend that you measure the total quantity and size of the particulates generated during the simulated use of your device. We recommend you perform particulate evaluation under the worst-case conditions of use. For example, for devices intended for ISR, we recommend that you evaluate the quantity and sizes of particulate generated from tracking the device through the tortuous path fixture and placement within a stent which has been deployed in the mock vessel.

Method Validation

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

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

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