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Standard Guide for Model Development for Particulate Generation Testing of Endovascular Devices¹

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1. Scope

1.1 This standard provides recommendations regarding the development of a simulated use model for particulate generation testing of endovascular devices.

1.2 Corresponding recommendations will be provided for the coronary, peripheral, and neurovascular anatomy respectively, as these different environments each have unique challenges and considerations that should be incorporated into the model development.

1.3 Considerations include, but are not limited to: anatomical considerations (for example, tortuosity, dimensions, disease state), working path length of the human vasculature, model/device interactions (for example, material properties, vessel straightening due to device placement), and device/device interactions (for example, use of delivery catheters and/or guide wires).

1.4 Standardizing the model development allows for better interpretation of the test results and comparison of performance of similar medical devices.

1.5 Explicit models for devices (or groups of devices) are not provided in this document as specific device attributes (for example, device flexibility, device material), anatomical target locations, and intended patient population can strongly impact model design. This document enables the development of a model that appropriately and sufficiently challenges the subject device with respect to particulate generation.

1.6 While this document is intended to aid in the development and design of the simulated use model for the assessment of particulate generation, additional information regarding the evaluation of the particulate matter and particulate measurements can be found in AAMI TIR 42. Similarly, this document is not intended to address testing associated with the use of the model.

1.7 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the*

responsibility of the user of this standard to establish appropriate safety, health, and environmental practices and determine the applicability of regulatory limitations prior to use.

1.8 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.*

2. Referenced Documents

2.1 Other Standards:

Guidance for Industry and FDA Staff Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems, April 18, 2010²

Guidance for Industry and FDA Staff Coronary, Peripheral, and Neurovascular Guidewires—Performance Tests and Recommended Labeling, October 10, 2019²

AAMI TIR 42:2021 Evaluation of Particulates Associated with Vascular Medical Devices³

3. Terminology

3.1 Definitions:

3.1.1 *context of use (COU)*—defines the specific role and scope of the model used to address a question of interest.

3.1.2 *model credibility*—the trust, obtained through the collection of evidence, in the capability of a model for a COU.

3.1.3 *question of interest*—the specific question, decision, or concern that is being addressed.

3.1.4 *risk*—combination of the probability of occurrence of harm and the severity of that harm.

3.1.5 *simulated use model*—a model that simulates or replicates the vasculature path through which the vascular device will be navigated (that is, access site, tracking length, target location).

¹ This guide is under the jurisdiction of ASTM Committee F04 on Medical and Surgical Materials and Devices and is the direct responsibility of Subcommittee F04.30 on Cardiovascular Standards.

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² Available from U.S. Food and Drug Administration (FDA), 10903 New Hampshire Ave., Silver Spring, MD 20993, <http://www.fda.gov>.

³ Available from Association for the Advancement of Medical Instrumentation (AAMI), 4301 N. Fairfax Dr., Suite 301, Arlington, VA 22203-1633, <http://www.aami.org>.

4. Summary of Guide

4.1 This guide covers the development and design of a simulated use model for the purpose of evaluating particulate generation for endovascular devices.

4.2 As part of model development, this guide discusses elements regarding model credibility such as model geometry, physical parameters, and historical comparators all relevant to the device's intended use.

5. Significance and Use

5.1 The evaluation of particulates from endovascular devices is a critical parameter to help ensure that the devices can be delivered to and from the treatment site with minimal unintended effects due to particulate generation.

5.2 This guide is intended for the development and design of a simulated use model for the evaluation of particulate generation by those manufacturing and/or evaluating endovascular devices.

5.3 This guide may be useful for establishment of credibility of a simulated use model as part of development testing and regulatory submission testing and filings.

6. Procedure

6.1 *General Considerations*—Construction of the model should consider the clinically relevant and appropriately challenging pathway with tortuosity reflective of the intended use. Additional information regarding the clinical pathway and tortuosity information is contained in the relevant subsections below. The model should approximate the vessels that the interventional devices track through to reach the deployment site / target location. The particulate model developed should address the intended use of the device as it relates to the disease state. Depending on the device's intended use, different access sites (femoral, radial, and others) and relevant tracking pathways may need to be considered. Target site design features may also need to be considered for devices intended for specific disease states, such as vascular occlusions, or in-stent restenosis. Similar target site considerations to those provided in 6.5 may also need to be applied here. To support model credibility as discussed in 6.2, how the model represents an appropriately challenging clinical use environment for its intended use of the device should be discussed.

6.2 *Model Credibility*—A simulated use model that is used to assess particulate generation for endovascular devices should be demonstrated to be credible for the question of interest in the context of use. For the model to have appropriate credibility, it should represent appropriately challenging vessel diameters and tortuosity, with allowances to deviate based on the following: material properties, manufacturability, and ability to validate (spiking and recovery). Modifications to model diameter(s) and tortuosity may impact the device path and should be considered. For the purpose of this standard, a typical question of interest would be: Does my device, during initial clinical use, generate particulate matter at sufficiently low levels that harmful embolization is unlikely to occur? A typical COU could be: The *in vitro* model is intended to mimic the potential particulate generation associated with use of my

device in challenging anatomy associated with a reasonably high percentage of the expected patient population. Once the question of interest and context of use are defined, the embolic risk from particulate generation, as measured by simulated use testing in the model, may be assessed and evaluated for the specified vasculature. For example, a device intended for use in the neurovascular arteries may carry more patient risk for embolic or neurological complications with particulate generation than a device intended for use in the peripheral vasculature. Based on the risks associated with a device's use, increased model credibility may be needed. Model credibility can be enhanced by inclusion of multiple credibility factors in the design a single model. For example, in addition to potential *in vitro* testing with the model, animal testing may also be completed to assess the effects and establish the safety of particulate generation from the device under question. The level of model credibility established should be commensurate with the associated risk of particulate generation. Model credibility should be established using a rationale that considers credibility factor(s). A list of possible credibility factors is provided in Table 1.

6.2.1 *Material and Manufacturing Considerations for Model Development*—There are many materials that are available, each with its strengths and weaknesses. Proper selection of the model materials may impact the number of particles collected in multiple ways. Some materials may be more challenging to clean and may retain particles from prior testing or may be prone to generate additional particles. Particles generated from the model material may also impact the ability to identify and attribute particles released from the device. Additionally, the connections of the model with the rest of the system need to be engineered such that the connection can be made/undone with ease, remains leak-free during handling, and does not result in cracks in the model. If the model is maintained appropriately, it can last many testing campaigns without degradation. In addition to the considerations provided below, model development should also consider factors related to particulate collection, measurements, and quantification, as discussed in AAMI TIR 42.

6.2.1.1 *Glass*—Glass has long been used as the material of choice because of its transparency, formability, and ease of cleaning. Unfortunately, its rigidity does not mimic the compliance of vasculature. However, the rigidity does allow for the prevention of vessel straightening, which allows for a more challenging assessment regarding tortuosity. Manufacturing of glass models can be challenging, especially if the geometry includes significant helicity and/or branching. If the manufacturing process requires manual steps, repeatability of the model dimensions can include significant variability.

6.2.1.2 *Silicone*—Silicone and other compliant materials can be cast accurately and can provide compliance values within physiological ranges; however, the interfacial friction can be significantly higher than anatomically relevant tissue. Interfacial friction can also limit device deliverability as well as cause inaccurate particulate counts from both the model and the devices being evaluated. The material properties make the model harder to clean and harder to get an appropriate baseline count before or in between testing. Depending on the types of