

MEDICAL DEVICE AND DIAGNOSTIC INDUSTRY

## Catheters and Stents

# The Evolution of Coatings for Endovascular Devices

Manufacturers no longer have to choose between low-particulate and low-friction coatings.

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**H**ydrophilic coatings are often used to improve access for delivery and placement of endovascular devices such as catheters. These coatings increase a device's lubricity, which reduces the frictional forces between the device and other devices or the vascular tissue itself. Hydrophilic coatings were traditionally evaluated by measuring sliding force, such as coefficient of friction, and durability through repeated cycling. While those measures of lubricity and durability are still used, today coatings are subjected to a newer performance parameter: particulate generation.

In recent years, regulators have increasingly asked medical device manufacturers to evaluate particulate generation associated with their devices' manufacture and use. As a result, many device developers now consider particulate reduction an important design criterion during product development and include evaluations of particulates in their hydrophilic coatings as part of internal testing. While interest in particulates—whether generated during manufacture or use in a procedure—is not new, more attention is being paid to the variables that could contribute to particulates. Manufacturers are now considering improved coatings, methods for assessing particulate generation related to devices, and ways to actively reduce particulates.

For device coatings manufacturers, the ability to lower particulate generation as an independent performance specification



**A coronary simulated-use model is used to evaluate both friction and particulate properties of a PTCA catheter.**

is fairly straightforward. The challenge comes in minimizing particulates while optimizing coating lubricity. Tradeoffs come with pairing the two performance requirements. Historically, this combined performance specification has been difficult for technology developers to overcome. However, recent advances in technology have enabled the development of improved coating options that deliver excellent lubricious characteristics in low-particulate formulas. This article summarizes the considerations to keep in mind when evaluating lubricious coatings for endovascular devices.

### Coating Purposes and Properties

Medical device coatings serve three main functions: active therapy, passive therapy, and access. Active therapy coatings enable therapeutic agents to be delivered to the treatment site. This has the advantage of targeting the agent to the area of the body where it is needed most while reducing the systemic concentration, which may cause undesired side effects. Active agents can be delivered from the coatings by diffusion from the coating, swelling of the coating matrix, or degradation of the coating material. In contrast, passive therapy coatings do not deliver an active agent. Their material properties provide benefits such as reduced thrombogenic potential, minimal inflammatory response, and enhanced growth of certain cells on the surface of the device. When evaluating active and passive therapy coatings, consider the specific requirements of

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## Coatings that are both low-particulate and low-friction are now available.

the coating and device, such as drug-release rate for an active coating or improved blood compatibility for a passive coating.

Obviously, any therapeutic or diagnostic endovascular device must reach the target site before treatment can begin. Access coatings make it easier for medical devices to reach the treatment site. While oils or polytetrafluoroethylene (PTFE) can reduce friction somewhat, hydrophilic hydrogel coatings can exhibit dramatic reductions (10–100 fold) in frictional forces because they can absorb large amounts of water, in many cases more than 90% by weight.<sup>1</sup> The water acts as a lubricant, so the device has a water layer between it and the surrounding device or tissue.

### Coating Friction Evaluations

The same water uptake property that enables extreme lubricity from hydrogel coatings also makes the coatings susceptible to mechanical failure if subjected to sufficient force. Testing hydrogel coatings during product development and manufacturing can demonstrate that the coatings have appropriate friction-reducing properties and mechanical integrity.

The lubricity of hydrogel coatings has been measured in many ways, but there are two main techniques. A friction tester applies a known force or load to the coated device and then measures the force needed to move the device. Loads can be applied by squeezing the device between two pads or putting an appropriate weight on a sled that rides on the device. Alternatively, the device can be passed through a simulated-use model with a number of turns and bends. The force needed to advance and retract the device through the pathway can then be measured. While the force applied to the coating is unknown in this test method, it evaluates the device in pathways that may simulate the tortuosity of the vascular anatomy. It is important to note that the materials used in the test pathway may be harder and less flexible than actual vessels, and could subject



**Solution collected from a simulated-use model is placed in a particle detection system to count and size the particulate generated.**

the medical device to a different level of stress than would be seen in the body. Supplemental in vivo test methods may also be considered for this reason.

With either frictional test method, repeated cycling of the device through the test apparatus can be used to evaluate the coating's durability. Coatings that are not durable will wear off, and the force needed to move the device through the test fixture will increase. Good lubricious coatings usually show a greater than 90% reduction in frictional forces compared with an uncoated device and will maintain that lubricity over many cycles of the frictional test method.

Another aspect of coating integrity is the amount and size of the hydrogel particles generated when the coating is subjected to stress. However, particulate test methods and guidances for medical devices are not well defined.

### Regulatory Guidance

Concerns about particulates from medical devices used in the vasculature include the risk of downstream emboli. As a result, there has always been interest in reducing the amount of particulates generated in a procedure. Device design, materials, clinical location, and procedural technique can all affect the amount and size of particulates generated. Several standards and guidance documents cover the evaluation of coatings for medical devices; however, no existing specifications or defined tests regarding particulates are entirely applicable for those generated from medical devices.

The U.S. Pharmacopeial Convention's chapter <788>, "Particulate Matter in Injections," is often referenced and describes methods to count particulates in solution.<sup>2</sup> It defines limits for the quantity of particles that are >10  $\mu\text{m}$  and >25  $\mu\text{m}$  per 1 ml of solution and provides instructions for counting the particles. However, the chapter does not provide guidance on how to generate a sample from the medical device or explain what an acceptable threshold of particles generated from a medical device should be.

An AAMI technical information report describes the evaluation of particulates from medical devices, covering particulates from many sources, not just coatings. It describes test methods for collecting particulate matter and considerations for the various sources and evaluation of particulates. The report states, "the literature does not provide discrete thresholds to establish safety limits for particulate load."<sup>3</sup>

ASTM F2394 describes how to evaluate the securement of a stent mounted on a delivery system.<sup>4</sup> It shows test pathways that may be relevant to testing stent delivery systems. ASTM F2743 is a test method for evaluating coatings and particulate characterization of drug-eluting stent systems.<sup>5</sup> However, like the AAMI technical information report, it does not provide specific recommendations for the test method or acceptance criteria.

The FDA guidance document for percutaneous transluminal coronary angioplasty (PTCA) catheters includes a section dedicated to particulate evaluation.<sup>6</sup> It recommends counting and reporting particles in at least three sizes ( $>10\ \mu\text{m}$ ,  $>25\ \mu\text{m}$ , and at a minimum  $>50\ \mu\text{m}$ ) using an appropriate simulated-use model. It does not establish acceptance criteria for the level of particulates but recommends providing an interpretation of the test data during device submission. As a result, device manufacturers are responsible for developing an appropriate particulate evaluation procedure.

It is important to acknowledge that while lubricious coatings with reduced particulate generation are preferred, lubricious coatings have been used commercially for more than 20 years with well-established benefits such as reduction of tissue trauma, improved maneuverability, and reduced procedure times.<sup>7</sup>

its composition and how it will be cleaned and prepared prior to sample collection. Likewise, determine and standardize the sample storage conditions, such as temperature and humidity, prior to analysis as much as is practical.

Choose the method of particle detection with an understanding of the advantages and drawbacks of each method. The most common particle detection methods are light obscuration and electrozone testing. Both are indirect measurement methods in that they do not directly visualize the particles. Light obscuration measures changes in refractive index and electrozone testing measures changes in electrical impedance as the particles flow through an aperture.

It is important to establish how particulates will be measured and keep the test method consistent throughout the evaluation process. Variations in testing methodology make it difficult to accurately compare results from different test runs.

### Recent Advancements

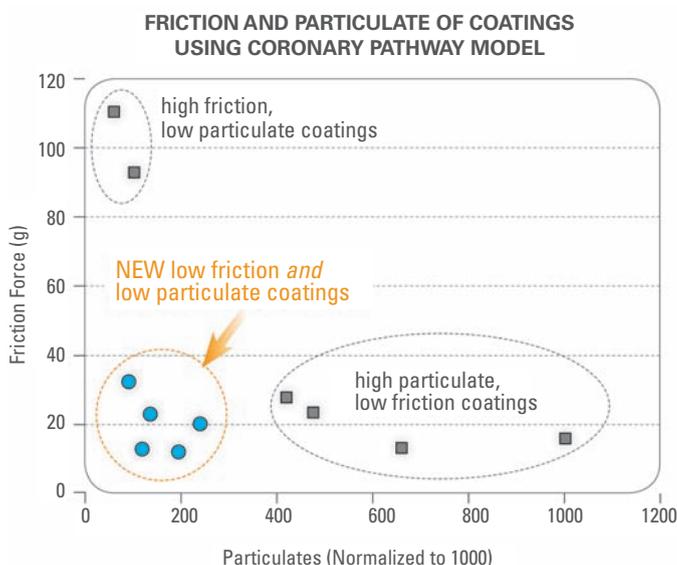
In the past there has often been a trade-off between the amount of particulates generated from a hydrophilic coating and the lubricity of that coating. Coatings that were more heavily cross-linked had greater mechanical strength but at the cost of reduced water uptake, which limited their lubricity. This trade-off between high lubricity and low particulates in a medical device coating is no longer necessary.

Medical device manufacturers can now select hydrophilic coatings that maintain their friction-reducing nature while minimizing the amount of hydrogel particulate generated from the coating during use. Figure 1 shows the relationship between friction and particulates for both previous and new-generation coatings. Some previous coating formulations had an inverse relationship between their frictional force and the amount of particulates generated. The low friction and low particulates of the most current coatings allow for easier access and improve safety.

While studies on the use of materials for therapeutic embolization have been published, few preclinical studies have examined the effect of hydrogel particulates in the vascular system.<sup>8</sup> A recent *in vivo* study that did so characterized hydrogel particulates and the accompanying potential for adverse effects.<sup>9</sup> This study evaluated PTCA catheters with two coatings of different thicknesses and levels of bench-top particulate formation. Histologic examination showed no evidence of particulates in either the myocardial tissue or downstream organs after treatment with the catheters with the thinner, lower particulate coating and only rare instances of hydrogel particulates from tissue treated with the thicker coating. As a result, study pathologists found no safety concerns with either coating.

### Conclusion

Particulate characterization is a new aspect of medical device evaluation. Hydrophilic coatings have traditionally been evaluated by a combination of friction and durability testing. Particulate testing should now be considered when developing a new coated medical device. While guidance documents state that particulates from medical device coatings should be characterized and evaluated, there is no defined test or specification regarding



**Figure 1.** This graph shows the relationship between friction and particulate generation of older (gray) and newer coatings (blue).

### Measurement of Particulates

Given the need to measure particulates from coated medical devices without specific guidance on how to perform the testing, it is important to consider how the sample will be generated, collected, and measured as a particulate test regimen is set up.

Choose the test pathway, or simulated-use model, based on clinical relevance. For example, consider the degree of tortuosity and luminal diameter of the vessels in the clinical application and material composition as the test system is developed. Also, determine delivery and deployment techniques of the device through the test model.

The sample collection container should be specified both for

particulates for medical devices. When setting up a particulate test method, care should be given to how test samples will be generated, collected, and detected. Recent advances in coating technology have eliminated the need to choose between good lubricity and low particulates. Coatings that are both low-particulate and low-friction are now available and are one more option for medical device makers who seek to reduce potential particulate generation.

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## About SurModics

As the world leader in medical device coatings, SurModics technology provides enhanced performance to more than 150 commercial device families in the following categories: cardiovascular, diabetes, gastrointestinal, neurology, obesity, oncology, and urology. SurModics partners with market-leading medical device manufacturers that value SurModics' performance, clinical, regulatory and manufacturing advantages.

SurModics' extensive knowledge of hydrophilic, lubricious coatings has led to a recent breakthrough in this category. With growing regulatory awareness of particulate generation, the new Serene™ coating platform delivers lubricity and durability while significantly reducing particulates. This next-generation coating has demonstrated excellent lubricity on a wide range of substrates, and has been used on FDA-cleared coronary and peripheral devices.

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