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# Intravascular Catheters, Wires, and Delivery Systems with Lubricious Coatings - Labeling Considerations

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# Guidance for Industry and Food and Drug Administration Staff

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For questions about this document, contact OHT2: Office of Cardiovascular Devices at (301) 796-7000 or OHT5: Office of Neurological and Physical Medicine Devices at (301) 796-6610.




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

# Preface

## Public Comment

You may submit electronic comments and suggestions at any time for Agency consideration to https://www.regulations.gov. Submit written comments to the Dockets Management Staff, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852. Identify all comments with the docket number FDA-2018-D-1774. Comments may not be acted upon by the Agency until the document is next revised or updated.

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***This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.***

## I. Introduction

This guidance document addresses labeling considerations for devices containing lubricious coatings used in the vasculature. The purpose of this guidance document is to provide recommendations for information to be included in the device labeling, as submitted in premarket applications (PMAs) or premarket notification submissions (510(k)s) for Class III and Class II devices, to enhance the consistency of coating-related information across these product areas, as well as to promote the safe use of these devices in the clinical setting. Medical devices such as intravascular catheters, guidewires, balloon angioplasty catheters, delivery sheaths, and implant delivery systems are commonly used during minimally invasive diagnostic and therapeutic procedures in the cerebrovascular, cardiovascular, and peripheral vascular systems. These devices often have hydrophilic and/or hydrophobic lubricious coatings (e.g., polyvinylpyrrolidone (PVP), polytetrafluoroethylene (PTFE), silicone) to reduce friction between devices, and between device(s) and blood vessels. It is commonly believed that these coatings may offer physicians greater maneuverability and may result in less trauma to blood vessels for patients.

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

# II. Background

Hydrophilic and/or hydrophobic coated devices have been used for more than 20 years in minimally invasive diagnostic and therapeutic cerebrovascular, cardiovascular, and peripheral vascular procedures. Both of these types of coatings decrease friction between the device and blood vessels. These devices facilitate the ability for physicians to provide minimally invasive treatment options to patients.

Although these devices may offer patient benefits, recent evidence indicates that the coating may separate from intravascular devices in some circumstances. The FDA has received and analyzed information concerning serious adverse events associated with hydrophilic and/or hydrophobic coatings separating (e.g., peeling, flaking, shedding, delaminating, sloughing off) from intravascular medical devices. This information has included voluntary recalls of guidewires, sheaths, retrieval devices, and embolization device delivery wires, as well as Medical Device Reports (MDRs) describing separation of hydrophilic and/or hydrophobic coatings from medical devices such as guidewires, catheters, and introducers that have been used for cerebrovascular, cardiovascular, and peripheral vascular procedures.

The FDA has also evaluated other relevant information, including peer-reviewed medical literature[1,2,3,4] and physician surveys[5]. Serious adverse events reported in these MDRs and in the medical literature include pulmonary embolism, pulmonary infarction, myocardial embolism, myocardial infarction, embolic stroke, tissue necrosis, and death. Serious injuries associated with the peeling of coatings reported in MDRs included the persistence of coating fragments in patients, some of which required surgical intervention to mitigate the consequences, adverse tissue reactions, and thromboses. Additional information related to these analyses may be found in the FDA Safety Communication for Lubricious Coating Separation from Intravascular Medical Devices issued on November 23, 2015 (http://wayback.archive-it.org/7993/20170722215712/https://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm473794.htm). This safety communication was issued to make health care providers aware of the possibility that hydrophilic and/or hydrophobic coatings may separate from medical devices

[1] Grundeken MJ, Li X, Kurpershoek E, Kramer MC, Vink A, Piek JJ, Tijssen JGP, Kock KT, Wykrzykowska JJ, de Winter RJ, van der Wal AC, Distal Embolization of Hydrophilic-Coating Material From Coronary Guidewires After Percutaneous Coronary Interventions. Circulation: Cardiovascular Interventions, 2015; 8(2):e001816.

[2] Hu YC, Deshmukh VR, Albuquerque FC, Fiorella D, Nixon RR, Heck DH, Barnwell SL, McDougall CG, Histopathological assessment of fatal ipsilateral intraparenchymal hemorrhages after the treatment of supraclinoid aneurysms with the Pipeline Embolization Device. Journal of Neurosurgery, 2014; 120(2); 365-374.

[3] Mehta RI, Mehta RI, Choi JM, Mukherjee A, Castellani RJ, Hydrophilic polymer embolism and associated vasculopathy of the lung: prevalence in a retrospective autopsy study. Human Pathology, 2014; 46(2): 191-201.

[4] Mehta RI, Mehta RI, Chung YC, Hydrophilic polymer embolism: an underrecognized iatrogenic cause of ischemia, inflammation, and coagulopathy. Human Pathology, 2015; 46(3): 488-489.

[5] MedSun Newsletter. (2015, Oct). Hydrophilic Coating and Hydrophobic Coating on Medical Devices Used in the Vasculature." 15(2), 3-11. (http://wayback.archive-it.org/7993/20170112002248/http://www.fda.gov/downloads/MedicalDevices/Safety/MedSunMedicalProductSafetyNetwork/Newsletters/UCM464550.pdf)

and potentially cause serious injuries to patients. The safety communication also includes information physicians may consider to reduce the potential of adverse events.

The FDA has not concluded that any specific manufacturer or brand of these devices is associated with higher risks than others. The cause of coating separation is multifactorial, and can be associated with factors including device design, device manufacturing (including formulation and raw material sourcing) and clinical use. Current FDA analysis suggests that clinical use-related issues may be mitigated through proper device selection, preparation, adequate premarket testing and other labeling considerations that are addressed within this guidance document. For recommendations on premarket testing, please refer to the FDA guidance titled "Class II Special Controls Guidance Document for Certain Percutaneous Transluminal Coronary Angioplasty (PTCA) Catheters," [6] the FDA guidance titled "Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems"[7], and the guidance titled "Performance Tests and Recommended Labeling for Coronary, Peripheral, and Neurovascular Guidewires."[8]

# III. Scope

This guidance document provides labeling recommendations for both Class III and Class II devices such as intravascular catheters, wires, and delivery systems with lubricious coatings used in the vasculature. Due to higher risks that are associated with use of these devices in the neuro-, coronary, and peripheral vasculature, FDA has focused the scope of this guidance on devices used in those vascular regions, although some of these considerations could be applicable to devices with similar coatings used in other types of interventional procedures. The scope of this guidance document includes a variety of devices and product codes including the following Class II and Class III devices (Tables 1 and 2, respectively). The devices are listed in alphabetical order (not risk- or event-based).

**Table 1. Class II Devices Within Scope of Guidance**

| Product Code | Product Code Name | Regulation Number |
|---|---|---|
| DQO | Catheter, Intravascular, Diagnostic | 870.1200 |
| DQX | Wire, Guide, Catheter | 870.1330 |
| DQY | Percutaneous Catheter | 870.1250 |
| DSP | System, Balloon, Intra-Aortic and Control | 870.3535 |
| DXE | Catheter, Embolectomy | 870.5150 |
| DXO | Transducer, Pressure, Catheter Tip | 870.2870 |
| DYB | Introducer, Catheter | 870.1340 |

[6] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/class-ii-special-controls-guidance-document-certain-percutaneous-transluminal-coronary-angioplasty
[7] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/non-clinical-engineering-tests-and-recommended-labeling-intravascular-stents-and-associated-delivery
[8] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/coronary-peripheral-and-neurovascular-guidewires-performance-tests-and-recommended-labeling

| Product Code | Product Code Name | Regulation Number |
|---|---|---|
| FOZ | Catheter, Intravascular, Therapeutic, Short-Term Less Than 30 Days | 880.5200 |
| HCG | Device, Neurovascular Embolization | 882.5950 |
| KRA | Catheter, Continuous Flush | 870.1210 |
| LIT | Catheter, Angioplasty, Peripheral, Transluminal | 870.1250 |
| LJS | Catheter, Intravascular, Therapeutic, Long-Term Greater Than 30 Days | 880.5970 |
| LJT | Port & Catheter, Implanted, Subcutaneous, Intravascular | 880.5965 |
| LOX | Catheters, Transluminal Coronary Angioplasty, Percutaneous | 870.5100 |
| MCW | Catheter, Peripheral, Atherectomy | 870.4875 |
| MJN | Catheter, Intravascular Occluding, Temporary | 870.4450 |
| MOF | Guide, Wire, Catheter, Neurovasculature | 870.1330 |
| NDQ | System, Catheter or Guidewire, Steerable (Magnetic) | 870.1290 |
| NFA | Temporary Coronary Saphenous Vein Bypass Graft Catheter for Embolic Protection | 870.1250 |
| NRY | Catheter, Thrombus Retriever | 870.1250 |
| NTE | Temporary Carotid Catheter for Embolic Capture | 870.1250 |
| NVM | Catheter, Angioplasty, Peripheral, Transluminal, Dual-Balloon | 870.1250 |
| POL | Neurovascular Mechanical Thrombectomy Device for Acute Ischemic Stroke Treatment | 882.5600 |

Although the product codes listed above are current as of the date of issuance of this guidance, new product codes may be created over time for vascular medical devices regulated under the classification regulations identified and fall within the scope of this guidance. We recommend that you contact OHT2: Office of Cardiovascular Devices or OHT5: Office of Neurological and Physical Medicine Devices if you are unsure whether this guidance applies to your device or product code if it is not already captured in this guidance.

**Table 2. Class III Devices Within Scope of Guidance**

| Product Code | Product Code Name |
|---|---|
| MAF | Stent, Coronary |
| MIH | System, Endovascular Graft, Aortic Aneurysm Treatment |
| MLV | Transcatheter Septal Occluder |
| MOM | System, Hemodynamic, Implantable |
| NIM | Stent, Carotid |
| NIN | Stent, Renal |
| NIO | Stent, Iliac |

| Product Code | Product Code Name |
|---|---|
| NIP | Stent, Superficial Femoral Artery |
| NJE | Intracranial Neurovascular Stent |
| NKM | Mitral Valve Repair Devices |
| NPT | Aortic Valve, Prosthesis, Percutaneously Delivered |
| NWX | Catheter, Percutaneous Transluminal Coronary Angioplasty (PTCA), Cutting/Scoring |
| ONU | Drug-Eluting Peripheral Transluminal Angioplasty Catheter |
| OUT | Intracranial Aneurysm Flow Diverter |
| PFV | System, Endovascular Graft, Arteriovenous (AV) Dialysis Access Circuit Stenosis Treatment |
| QCA | Intracranial Coil-Assist Stent |

# IV. Recommended Labeling Considerations

This guidance is intended to help develop labeling that will provide information for use and other information in accordance with 21 CFR Part 801.109 and other applicable requirements in 21 CFR 801. FDA recommends including the following information in the device labeling for intravascular devices with lubricious coatings. We intend for this information to supplement and enhance the information that is already in the device labeling for these device types, and do not intend for it to replace information already included in the labeling. Since these recommendations are based on known safety issues, FDA recommends that this information be considered for inclusion as current product labeling is updated, and that labeling included as part of future premarket submissions for intravascular devices with lubricious coatings incorporate the recommendations. For currently 510(k)-cleared intravascular devices with lubricous coatings, please refer to FDA's guidance "Deciding When to Submit a 510(k) for a Change to an Existing Device,"[9] which provides guidance to 510(k) holders on deciding when to submit a 510(k) for a change to an existing device.

## A. Device Description

In addition to the device description currently provided for the device, the device labeling for a coated device should include a statement to identify that the device is coated, as well as a brief description (e.g., hydrophilic, hydrophobic) of the coating, its location on the device (e.g., proximal or distal end), the length of the coating, and its purpose.

We recommend the device description prominently note the presence of the coating and refer the user to additional critical information.

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

If the device is intended for use with specific ancillary device(s) dimension(s), we recommend specifying this information because size mismatch may result in coating damage and adverse events.

## B. Indications for Use Statement

All indications for use described in the labeling should be supported by information in the premarket submission. For intravascular devices, this includes identifying any specific regions of the vasculature for which the device is cleared or approved for use.

## C. Warnings, Precautions and Preparation Steps

Many devices are designed, labeled, and indicated for specific uses. FDA acknowledges that the specific warnings and precautions may depend on the specific design and intended use of the device. For example, the coating and performance of a device intended to be used in the peripheral vasculature may be different than a device intended to be used in the cerebral vasculature. If information regarding safety is not available or has not been established for indications other than those specified in the regulatory submission, it may be appropriate to consider the inclusion of a precaution statement reflecting such. For example: "The safety and effectiveness of the coated device has not been established, or is unknown, in vascular regions other than those specifically indicated."

In addition, we recommend that the labeling include any other specific considerations such as device compatibility, storage conditions, specific preparation steps, and any appropriate troubleshooting or tips that should be conveyed to the device user in order to enhance the safe use of the device. Table 1 provides a listing of the information suggested for inclusion.

The preparation steps should include information that will guide the user in a clinical setting. Some of these items may be included as warnings or precautions in the instructions for use or on the outer label. Please refer to Table 1 for specific recommendations to consider when developing the labeling. If you believe one or more of these considerations are not applicable to your device, we recommend you provide a brief rationale in your premarket submission. We recommend that you include any additional warnings and precautions not identified below that you determine are necessary to promote the safe use of the device based on your device design and intended use.

| **Table 3. Recommendations and Items to Consider When Developing the Labeling** | |
|---|---|
| **Warnings and Precautions** | |
| a. | Any instructions, warnings, or precautions necessary to ensure the safe and effective use of the lubricious coating should be addressed. |
| b. | We recommend including a warning, such as: "Warning: Failure to abide by the warnings in this labeling might result in damage to the device coating, which may necessitate intervention or result in serious adverse events." |
| c. | We recommend a warning against reuse or re-sterilization of the device, which could damage the coating and affect coating performance, for example, "This device is intended for single use. Do not reuse or re-sterilize." |
| d. | If applicable, we recommend specification of the appropriate duration for pre-conditioning. If applicable, include a precaution against soaking for extended periods when the device is not in use. If the coating integrity or performance could be negatively impacted by extended soaking or pre-conditioning, we recommend alerting the user of the maximum soaking or pre-conditioning time. For example, alert the user to avoid pre-soaking devices for longer than instructed, as this may impact the coating performance. |
| e. | If applicable, we recommend a specification of any known incompatibility with specific media or solvents (e.g., alcohol or antiseptic). If the coating integrity or performance could be negatively impacted by preparation with incompatible media, we recommend including a precaution in the labeling alerting the user. |
| f. | If applicable, we recommend inclusion of a warning or precaution regarding the swelling behavior of the coating when exposed to aqueous media and any impact on device use. |
| g. | We recommend that the labeling instruct and warn users to use caution when manipulating, advancing and/or withdrawing these devices through needles, metal cannulas, stents, or other devices with sharp edges, or through tortuous or calcified blood vessels. Manipulation, advancement, and/or withdrawal past sharp or beveled edges may result in destruction and/or separation of the outer coating, which may lead to clinical adverse events, resulting in coating material remaining in the vasculature or device damage. This may result in adverse events (section D below) requiring additional intervention. |
| **Preparation Steps and Instructions for Use** | |

| **Table 3. Recommendations and Items to Consider When Developing the Labeling** | |
|---|---|
| h. | If the device is anticipated to be used with other devices and/or accessories, sufficient information to identify a safe combination of devices and/or procedure-specific components should be included due to abrasion between devices.<br>1) For example, it is important that the user is informed of key device dimensions (e.g., French size, inner diameter, outer diameter) and potential compatibility issues with other devices based on these key dimensions. A tight fit between the subject device and ancillary devices may exacerbate frictional forces during use which could contribute to unanticipated coating loss such as peeling, flaking, shedding, delamination, or sloughing off.<br>2) If the device coating swells when exposed to aqueous media (e.g., saline, heparinized saline), which could impact its use with other devices, we recommend communicating this in the instructions for use. |
| i. | We recommend that any special storage and/or handling conditions are described. For example, any storage conditions needed to ensure the integrity of the coating over the labeled shelf-life should be described (e.g., limits related to light exposure, temperature, and/or relative humidity during storage, expiration date). |
| j. | The device's expiration date should be included on the package label. The date should be presented in a format consistent with 21 CFR 801.18. |
| k. | We recommend the specification of appropriate conditioning media (e.g., normal saline, sterile water, or heparinized saline) prior to and during clinical use. It should be stated when solutions may not be interchangeable, for instance if different media could affect the hydrophilic and/or hydrophobic coatings differently; this is important because coatings may vary from the proximal to the distal end on a single device. |
| l. | We recommend that any practices that should be avoided during preparation or device use that could result in misuse scenarios or coating damage be identified. Some examples may include:<br>1) Avoid wiping the device with dry gauze as this may damage the device coating.<br>2) Avoid excessive wiping of the coated device.<br>3) Avoid using alcohol, antiseptic solutions, or other solvents to pre-treat the device because this may cause unpredictable changes in the coating which could affect the device safety and performance.<br>4) Avoid pre-soaking devices for longer than instructed, as this may impact the coating performance. |

| **Table 3. Recommendations and Items to Consider When Developing the Labeling** | |
|---|---|
| m. | If the distal tip of the device is flexible and designed to be shaped by the physician, the labeling should instruct the user of appropriate shape configurations and shaping techniques. If applicable, it should also inform the user that attempting to alter the shape of devices by bending, twisting, or similar methods beyond instructed methods may compromise the coating integrity and that damage to the coating may not always be noticeable to the naked eye. |
| n. | In the event that the device should not move freely, it may be appropriate to recommend that the user determine the source of resistance, exercise caution when removing the device and/or other components as a unit, and exchange the device for a new one to complete the procedure. |

For more information on warnings and precautions, please refer to the Device Labeling Guidance #G91-1 (blue book memo) (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/device-labeling-guidance-g91-1-blue-book-memo).

## D. Potential Adverse Events

Potential adverse events that could be attributed to coating loss should be described in the labeling. FDA acknowledges that the specific adverse events may depend on the specific design and intended use of the device. Such adverse events may include, but are not limited to:

- Sterile inflammation or granulomas at the access site
- Pulmonary embolism
- Pulmonary infarct
- Myocardial embolism
- Myocardial infarct
- Embolic stroke
- Cerebral infarct
- Additional surgical intervention
- Tissue necrosis, transient or long-lasting
- Death