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

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

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For questions about this document, contact the Division of Cardiovascular Devices at (301) 796-7000 or the Division 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

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I. Introduction

This draft guidance document addresses labeling considerations for devices containing lubricious coatings used in the vasculature.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FDA's guidance documents, including this draft guidance, do not establish legally enforceable responsibilities.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

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85 cited. The use of the word *should* in Agency guidance means that something is suggested or
86 recommended, but not required.

87 **II. Background**

88
89 Hydrophilic and/or hydrophobic coated devices have been used for more than 20 years in
90 minimally invasive diagnostic and therapeutic cerebrovascular, cardiovascular, and peripheral
91 vascular procedures. Both of these types of coatings decrease friction between the device and
92 blood vessels. These devices facilitate the ability for physicians to provide minimally invasive
93 treatment options to patients.

94
95 Although these devices may offer patient benefits, recent evidence indicates that the coating may
96 separate from intravascular devices in some circumstances. The FDA has received and analyzed
97 information concerning serious adverse events associated with hydrophilic and/or hydrophobic
98 coatings separating (e.g., peeling, flaking, shedding, delaminating, sloughing off) from
99 intravascular medical devices. This information has included voluntary recalls of guidewires,
100 sheaths, retrieval devices, and embolization device delivery wires, as well as Medical Device
101 Reports (MDRs) describing separation of hydrophilic and/or hydrophobic coatings from medical
102 devices such as guidewires, catheters, and introducers that have been used for cerebrovascular,
103 cardiovascular, and peripheral vascular procedures.

104
105 The FDA has also evaluated other relevant information, including peer-reviewed medical
106 literature^{1,2,3,4} and physician surveys⁵. Serious adverse events reported in these MDRs and in the
107 medical literature include pulmonary embolism, pulmonary infarction, myocardial embolism,
108 myocardial infarction, embolic stroke, tissue necrosis, and death. Serious injuries associated with
109 the peeling of coatings reported in MDRs included the persistence of coating fragments in
110 patients, some of which required surgical intervention to mitigate the consequences, adverse
111 tissue reactions, and thromboses. Additional information related to these analyses may be found
112 in the [FDA Safety Communication](#) for Lubricious Coating Separation from Intravascular
113 Medical Devices issued on November 23, 2015 ([http://wayback.archive-](http://wayback.archive-it.org/7993/20170722215712/https://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/uc)
114 [it.org/7993/20170722215712/https://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/uc](https://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/uc)

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>)

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115 [m473794.htm](https://www.fda.gov/oc/ohrt/ohrt-473794.htm)). This safety communication was issued to make health care providers aware of
116 the possibility that hydrophilic and/or hydrophobic coatings may separate from medical devices
117 and potentially cause serious injuries to patients. The safety communication also includes
118 information physicians may consider to reduce the potential of adverse events.

119
120 The FDA has not concluded that any specific manufacturer or brand of these devices is
121 associated with higher risks than others. The cause of coating separation is multifactorial, and
122 can be associated with factors including device design, device manufacturing (including
123 formulation and raw material sourcing) and clinical use. Current FDA analysis suggests that
124 clinical use-related issues may be mitigated through proper device selection, preparation,
125 adequate premarket testing and other labeling considerations that are addressed within this
126 guidance document. For recommendations on premarket testing, please refer to the FDA
127 guidance titled “Class II Special Controls Guidance Document for Certain Percutaneous
128 Transluminal Coronary Angioplasty (PTCA) Catheters”
129 ([https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm](https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm225145.htm)
130 [225145.htm](https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm225145.htm)), the FDA guidance titled “Non-Clinical Engineering Tests and Recommended
131 Labeling for Intravascular Stents and Associated Delivery Systems”
132 ([https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocu](https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071986.pdf)
133 [ments/ucm071986.pdf](https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071986.pdf)) and the draft guidance titled “Performance Tests and Recommended
134 Labeling for Coronary, Peripheral, and Neurovascular Guidewires”
135 ([https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocu](https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM610631.pdf)
136 [ments/UCM610631.pdf](https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM610631.pdf)), which when finalized, will represent the Agency’s current thinking on
137 this topic.

III. Scope

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

- 148
- 149 • DQO, Catheter, Intravascular, Diagnostic
- 150 • DQX, Wire, Guide, Catheter
- 151 • DQY, Percutaneous Catheter
- 152 • DSP, System, Balloon, Intra-Aortic And Control
- 153 • DXE, Catheter, Embolectomy
- 154 • DXO, Transducer, Pressure, Catheter Tip
- 155 • DYB, Introducer, Catheter
- 156 • FOZ, Catheter, Intravascular, Therapeutic, Short-Term Less Than 30 Days
- 157 • HCG, Device, Neurovascular Embolization

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- 158 • KRA, Catheter, Continuous Flush
- 159 • LIT, Catheter, Angioplasty, Peripheral, Transluminal
- 160 • LJS, Catheter, Intravascular, Therapeutic, Long-Term Greater Than 30 Days
- 161 • LJT, Port & Catheter, Implanted, Subcutaneous, Intravascular
- 162 • LOX, Catheters, Transluminal Coronary Angioplasty, Percutaneous
- 163 • MAF, Stent, Coronary
- 164 • MCW, Catheter, Peripheral, Atherectomy
- 165 • MIH, System, Endovascular Graft, Aortic Aneurysm Treatment
- 166 • MJN, Catheter, Intravascular Occluding, Temporary
- 167 • MLV, Transcatheter Septal Occluder
- 168 • MOF, Guide, Wire, Catheter, Neurovasculature
- 169 • MOM, System, Hemodynamic, Implantable
- 170 • NDQ, System, Catheter Or Guidewire, Steerable (Magnetic)
- 171 • NFA, Temporary Coronary Saphenous Vein Bypass Graft Catheter for Embolic
172 Protection
- 173 • NIM, Stent, Carotid
- 174 • NIN, Stent, Renal
- 175 • NIO, Stent, Iliac
- 176 • NIP, Stent, Superficial Femoral Artery
- 177 • NKM, Mitral Valve Repair Devices
- 178 • NPT, Aortic Valve, Prosthesis, Percutaneously Delivered
- 179 • NRY, Catheter, Thrombus Retriever
- 180 • NTE, Temporary Carotid Catheter For Embolic Capture
- 181 • NVM, Catheter, Angioplasty, Peripheral, Transluminal, Dual-Balloon
- 182 • NWX, Catheter, Percutaneous Transluminal Coronary Angioplasty (PTCA),
183 Cutting/Scoring
- 184 • OUT, Intracranial Aneurysm Flow Diverter
- 185 • PFV, System, Endovascular Graft, Arteriovenous (AV) Dialysis Access Circuit Stenosis
186 Treatment

IV. Recommended Labeling Considerations

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189 This draft guidance is intended to help develop labeling that will provide information for use and
190 other information in accordance with 21 CFR Part 801.109 and other applicable requirements in
191 21 CFR 801. FDA recommends including the following information in the device labeling for
192 intravascular devices with lubricious coatings. We intend for this information to supplement and
193 enhance the information that is already in the device labeling for these device types, and do not
194 intend for it to replace information already included in the labeling. Since these
195 recommendations are based on known safety issues, FDA recommends that this information be
196 considered for inclusion as current product labeling is updated, and that labeling included as part
197 of future premarket submissions for intravascular devices with lubricious coatings incorporate
198 the recommendations. For currently 510(k)-cleared intravascular devices with lubricous coatings,
199 please refer to FDA’s guidance “Deciding When to Submit a 510(k) for a Change to an Existing

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200 Device,”
201 ([https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocu](https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM514771.pdf)
202 [ments/UCM514771.pdf](https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM514771.pdf)) which provides guidance to 510(k) holders on deciding when to submit
203 a 510(k) for a change to an existing device.
204

A. Device Description

205
206 We recommend the device labeling include a statement to identify whether or not
207 the device is coated, as well as a brief description (e.g., hydrophilic, hydrophobic)
208 of the coating, its location on the device, and its purpose.
209
210

B. Indications for Use Statement

211
212 All indications for use described in the labeling should be supported by
213 information in the premarket submission. For intravascular devices, this includes
214 identifying any specific regions of the vasculature for which the device is cleared
215 or approved for use.
216
217

C. Warnings, Precautions and Preparation Steps

218
219 Many devices are designed, labeled, and indicated for specific uses. FDA
220 acknowledges that the specific warnings and precautions may depend on the
221 specific design and intended use of the device. For example, the coating and
222 performance of a device intended to be used in the peripheral vasculature may be
223 different than a device intended to be used in the cerebral vasculature. Please refer
224 to item (a) in Table 1 for example considerations for precautions related to
225 specific vascular regions.
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228 We recommend including a general warning, at the beginning of the labeling that
229 specifies that the device is coated (example in Table 1 item (b)). In addition, we
230 recommend that the labeling include any other specific considerations such as
231 device compatibility, storage conditions, specific preparation steps, and any
232 appropriate troubleshooting or tips that should be conveyed to the device user in
233 order to enhance the safe use of the device. Table 1 provides a listing of the
234 information suggested for inclusion.
235

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

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a.	<p>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 warning statement reflecting such. For example: “The safety and effectiveness of the device has not been established, or is unknown, in vascular regions other than those specifically indicated.”</p> <p>If a specific guidewire is only indicated for peripheral vascular use based on the information provided in the premarket submission, the device should include a warning that the safety and effectiveness of the device has not been established in the coronary vasculature or neurovasculature. This is because guidewires only demonstrated to be safe and effective for peripheral vascular use could cause serious adverse events if used in the coronary vasculature or neurovasculature.</p>
b.	<p>We recommend a warning regarding the presence of the coating referring to additional critical information, for example, “This device is coated with a hydrophilic coating at the proximal (or distal) end of the device for a length of [XX] cm. Please refer to Section [X] or Page [X] for further information on how to prepare and use this device to ensure it performs as intended. 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.”</p>
c.	<p>We recommend a warning against reuse or re-sterilization of the device, which could affect coating performance, for example, “This device is intended for single use. Do not reuse or re-sterilize.”</p>
d.	<p>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.</p> <ol style="list-style-type: none">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 or flaking.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.

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e.	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).
f.	The device's expiration date should be included on the package label. The date should be presented in a format consistent with 21CFR 801.18.
g.	If the device is intended for use in a certain vascular bed or blood vessel diameter range, we recommend specifying this information. Size mismatch may result in adverse events. This is particularly important for small vessels where vessel injury (such as, but not limited to, perforation and dissection) may occur.
h.	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.
i.	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.
j.	If applicable, we recommend a specification of any 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.
k.	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.

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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: <ol style="list-style-type: none">1) Avoid wiping the device with dry gauze as this may damage the device coating.2) Avoid excessive wiping of the coated device.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.4) Avoid pre-soaking devices for longer than instructed, as this may impact the coating performance.
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.	We recommend that the labeling instruct that the user should avoid manipulating, advancing, and/or withdrawing the coated guidewire through a metal cannula or needle. Manipulation, advancement, and/or withdrawal through a metal device may result in destruction and/or separation of the outer coating, resulting in coating material remaining in the vasculature, which may result in unintended adverse events (section D below) requiring additional intervention.
o.	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.

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For more information on warnings and precautions, please refer to the Device Labeling Guidance #G91-1 (blue book memo) (<http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm081368.htm>).

D. Adverse Events

Any probable 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

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- 260 • Pulmonary embolism
- 261 • Pulmonary infarct
- 262 • Myocardial embolism
- 263 • Myocardial infarct
- 264 • Embolic stroke
- 265 • Cerebral infarct
- 266 • Tissue necrosis
- 267 • Death
- 268

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