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Off-Label Communications and The New Intended Use Regulations

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Off-Label Communications and The New Intended Use Regulations

After a nearly five-year delay, FDA's new "intended use" rule, 21 CFR § 801.4, finally became effective on September 1, 2021. Under the new rule, FDA clarifies the types of evidence relevant to determining the intended use of a medical device under the Food, Drug & Cosmetic Act. Although some commentators have opined the new rule will increase exposure for drug and device manufacturers regarding off-label communications, we do not believe the amendment represents a material change drug and device manufacturers in 2022 for at least three reasons.

First, the new intended use rule does not stake out any new enforcement authority for FDA. Contrary to most new regulations, the new intended use rule does not represent an expansion of FDA's authority. Instead, FDA has explained that it simply codified its prior approach regarding the evidence relevant to determining a product's intended use. ***Specifically, the new intended use regulation provides examples of the types of evidence that FDA may use to determine the intended use of a manufacturer's products for the purposes of regulatory or civil action and/or criminal enforcement.*** Importantly, and notwithstanding the new rule, FDA continues to assert it is not limited to statements made by the manufacturer in determining intended use. FDA reaffirms it can establish a product's intended use based on knowledge of the following: actual use by customers, consumer conduct, the environment in which the product is sold, the absence of labeling, witness testimony, training programs, internal documents and financial arrangements, to name a few evidentiary sources.

Second, the new intended use rule limits enforcement based upon mere knowledge of off-label use. The concern with prior iterations of 21 CFR § 801.4 was that a manufacturer's mere knowledge of an off-label use by a health care provider (and that knowledge alone) could either (1) create an affirmative obligation for the manufacturer to provide information (called

"adequate labeling") about those uses; or (2) subject the manufacturer to enforcement for off-label uses. This was a difficult burden for manufacturer's to accept given that the mere awareness of an off-label use could have been used by FDA to enforce off-label promotion. However, the recent amendments to Section 801.4 amend the regulation to confirm ***that a manufacturer's "mere knowledge" of an unapproved use cannot, in and of itself, establish a new intended use for prosecution purposes.*** Instead, FDA may consider such knowledge — along with other factors — as evidence of intended use, but cannot rely on mere knowledge alone. Although this change may ease some concern, manufacturers must remain mindful that FDA continues to possess substantial discretion in enforcing the off-label use or promotion of a medical device or drug. Moreover, if a manufacturer has knowledge of an off-label use then it is likely FDA also has that knowledge and can identify other factors to support an off-label use prosecution.

Finally, FDA's enforcement authority remains restricted by the First Amendment protections. For years, FDA has asserted that even if off-label promotional speech is truthful speech otherwise protected by the First Amendment, FDA can independently prosecute it as adulterated and misbranded the use was not approved. And just as frequently as FDA has made that argument, the courts have rejected it finding that truthful speech cannot be the basis for a civil violation or criminal prosecution. As a result, FDA has increasingly accepted off-label communications and begrudgingly accepted off-label promotion with appropriate disclosures/disclaimers to make it truthful and non-misleading. In fact, dissemination of literature about off-label uses is permitted under two current FDA guidance documents: "Responding to Unsolicited Requests for Off-Label Information about Prescription Drugs and Medical Devices" (December 2011), and "Distributing Scientific and Medical Publications on *Unapproved New Uses – Recommended Practices – Revised Guidance*," (February 2014).

FDA's more recent guidance entitled "Medical Products Communications That Are Consistent With the FDA-Required Labeling—Questions and

Answers," (June 2018), states that "[i]f a firm communicates information that is not contained in its product's FDA-required labeling but that is determined to be consistent with the FDA-required labeling, FDA does not intend to rely on that communication to establish a new intended use." *Thus, while the new "intended use" regulation permits FDA to rely upon a single piece of evidence to demonstrate a new, off-label intended use and prosecute a manufacturer, we do not believe the regulation materially affects FDA's enforcement of off-label promotion*. After all, the First Amendment remains the polestar when evaluating the lawfulness of off-label communications, and operates as a restriction with respect to FDA's enforcement authority.

After considering the new intended use regulation and the landscape of off-label promotion, we do not believe much has changed with the amendment to Section 801.4. While there may be some initial growing pains associated with the amended Section 801.4, and even some expansion of FDA's authority under the new provision, the amendments were intended to clarify, and not change, the definition of intended use. Indeed, FDA's own comments affirm this conclusion. (See 86 FR 41383) ("FDA is finalizing amendments to its intended use regulations for medical products . . . to better reflect the Agency's current practices in evaluating whether a product is intended for use as a drug or device, including whether a medical product that is approved, cleared, granted marketing authorization or exempted from premarket notification is intended for a new use.") *Therefore, although there was a five-year delay in implementing the amended regulation, we do not believe the amendments to Section 801.4 will materially change off-label communications in 2022 or beyond.*

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Drug, Device and Food Law

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