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FDA Proposes Modified "Intended Use" Regulations

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In its latest effort to provide direction and clarity to regulated industry and stakeholders, on September 23, the U.S. Food and Drug Administration (FDA) published a proposed rule and preamble amending its medical product "intended use" regulations "regarding the types of evidence that are relevant in determining a product's intended uses."[1] This proposal would repeal and replace portions of the controversial 2017 "final rule" — delayed, in part, based on industry's concern over FDA's proposed "totality of the circumstances" test to determine if a company intended for its product to be used "off-label." Notably, the 2020 proposed rule makes clear that it is not illegal for firms[2] to have knowledge, alone, that its product is being used "off-label," unless there is other objective evidence of intent. However, while the controversial "totality of circumstances" language has been deleted, FDA, in the preamble, states that it will continue to take different circumstances into account.

FDA's 2015 Proposed Rule and 2017 "Final Rule"

FDA's effort to bring clarity to its intended use regulations is not new as it previously issued a proposed rule in 2015[3] and a "final rule" in 2017.[4]

This earlier effort evoked industry concern because it proposed to establish a "totality of the evidence" test to determine a product's intended use. In addition, firms also expressed concern — through a petition[5] and in commentary to the proposed rule — that the last sentence of the 2017 final rule could mean "that a firm's mere knowledge of an unapproved use of its approved drug product automatically triggers requirements for new labeling that in turn renders distribution of that approved product unlawful without approval of a supplemental application."[6] Firms further expressed First Amendment concerns about how a product's intended use would be established and the potential use of knowledge as a category of evidence that may be considered as evidence.

Subsequently, FDA delayed the effective date of the "intended use" amendments, and they were never implemented.

2020 Proposed Rule

In announcing the proposed rule, FDA emphasized that it does not reflect a change, but serves only to clarify the language and "better reflect [FDA's] current practices in evaluating whether a product is intended for use as a drug or device, including whether an approved or cleared medical product is intended for a new use."

The preamble provides examples of the types of evidence that can be used to determine whether a drug or device is intended for use as an FDA drug or device or for an "off-label" or unapproved use, revising §§ 201.128 and 801.4. Conforming to FDA's longstanding practice, the rule remains very broad, allowing "any relevant source of evidence" to be considered. This includes direct and circumstantial evidence, but not necessarily subjective evidence of intent. FDA identifies the following as evidence relevant to establishing intended use:

- Express claims and representations:
  - product labeling
  - promotional claims
  - advertisements
  - oral or written statements by persons responsible for the labeling or their representatives
- Implied claims made by the firm that "implicitly represent a product for a particular use":
  - suggestive product names
  - statements that imply an intended use
  - representations about a particular ingredient implying some physiological effect
- Product characteristics and design:
  - known physiological effects of a product unapproved for medical use
  - known recreational or medical use of a product unapproved for any medical use
  - product's unique design or technical features
- Circumstances of sale or distribution

Although underscoring that the analysis is fact-specific, FDA enumerates a non-exhaustive list of examples in its proposed rule that, standing alone, are not determinative of intended use, including the following:

- Dissemination of safety information to health care providers to minimize the risk to patients;
- A firm's social media account that "follows," without commentary or endorsement, the social media account of nonprofit entities that support patients with a condition for which the firm has a product under investigation;

- Corporate filings regarding development or potential or actual sales of unapproved use;
- Internal documents reflecting potential sales of an unapproved use widely recognized as a standard of care; and
- Clinical trial summary information distributed solely to participants, that does not make conclusions on an unapproved product's safety or efficacy and includes a prominent and conspicuous disclaimer not approved, cleared, or licensed by FDA.

FDA's proposed rule further clarifies that knowledge alone will not support a finding of an intended use by deleting the last sentence of §§ 201.128 and 801.4. In its place, a new clause is added, stating that "a firm would not be regarded as intending an unapproved new use for an [approved or cleared medical product] based solely on that firm's knowledge that such [product] was being prescribed or used by health care providers for such use." This revision seemingly obviates the requirement to update labels for unapproved uses in circumstances where a firm only has knowledge that health care providers are exercising independent judgment to prescribe the product for unintended purposes.[7]

Additionally, in the preamble, FDA pushed back on the First Amendment concerns previously raised by firms, stating that knowledge and speech are not coextensive.[8] FDA expressed concern that if it relied "exclusively on firms' claims to establish intended use" — as the comments to the 2015 proposed rule suggested — this loophole would enable firms to evade FDA oversight, allowing marketing of products unapproved for any medical use. FDA maintains that existing policy and practice already allows it to rely on evidence other than express claims to establish intended use and "take into account any circumstances surrounding the distribution of the product or the context in which it is sold."

FDA further argues that the 2020 proposed rule, if finalized, is consistent with First Amendment principles for three reasons: 1) the proposed rule is limited in scope as it describes evidence that "may be relevant" to establishing intended use, not evidence that "will be determinative" of intended use; 2) the proposed rule does not affect the exclusions explicitly provided by statute or regulation from the drug or device definitions; and 3) the proposed rule does not reflect a change in FDA's policies and practices regarding the types of communications that would not, on their own, establish a firm's intent for a drug or device to be used "off-label." Moreover, FDA relies on decisions by the Supreme Court followed by the D.C. Circuit, holding that the government's reliance on speech as evidence of intended use under the Federal Food, Drug, and Cosmetic (FD&C) Act does not violate the First Amendment. Specifically, FDA points to *Wisconsin v. Mitchell*, 508 U.S. 476, 489 (1993), which held that "[t]he First Amendment . . . does not prohibit the evidentiary use of speech to establish the elements of a crime or to prove motive or intent."[9]

Client Considerations

In its preamble to the proposed rule, FDA provides some clarity and safe harbor examples that should help guide firms with knowledge that health care providers are using or prescribing their products for an unapproved use. However, for critics of the 2017 rule, FDA makes clear that it intends to continue evaluating different circumstances to evaluate whether a product has an intended use that has not been approved, even if they have

not articulated a specific "totality of circumstances" test. Moreover, FDA has not backed down from its position that it has the power to prosecute firms for off-label promotion, and that the First Amendment does not bar those prosecutions.

FDA is accepting comments on the proposed rule until October 23, 2020.

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[1] FDA, Proposed Rule, *Regulations Regarding "Intended Uses,"* 85 Fed. Reg. 59718 (Sep. 23, 2020) [hereinafter "*2020 Proposed Rule*"].

[2] "Firms" refers to manufacturers, packers, and distributors of FDA-regulated products and all their representatives, including both individuals and corporate entities.

[3] FDA, Proposed Rule, *Clarification of when Products Made or Derived from Tobacco Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding "Intended Uses,"* 80 Fed. Reg. 57756 (Sep. 25, 2015).

[4] FDA, Final Rule, *Clarification of When Products Made or Derived from Tobacco Are Regulated as Drugs, Devices, or Combination Products; Amendments to Regulations Regarding "Intended Uses,"* 82 Fed. Reg. 2193 (Jan. 9, 2017).

[5] *See* Docket No. FDA-2015-N-2002-1977.

[6] *2020 Proposed Rule*, 85 Fed. Reg. at 59718.

[7] There was some ambiguity in the past regarding when tobacco products would be regulated under FDA drug, device, or combination product regulations. The proposed rule seeks to clarify the interplay between intended use regulations and the tobacco regulations by inserting a reference to § 1100.5 in both §§ 201.128 and 801.4.

[8] *2020 Proposed Rule*, 85 Fed. Reg. 59722.

[9] *Id.* (citing *Wisconsin v. Mitchell*, 508 U.S. 476, 489 (1993)).

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