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Client Alert

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FDA Grants One-Year Extension on Intended Use Rule

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The Food and Drug Administration (FDA) has announced a one-year extension of a rule related to what pharmaceutical and device manufacturers can say about unapproved uses of their products, from March 21, 2017, until March 19, 2018. *See* March 17, 2017 FDA Clarification Notice ("Notice"), at 1; *see also* February 8, 2017 Petition and Stay for Reconsideration ("Petition"), at 12. The notice is available here.

Background

In 2015, the FDA proposed a change to the "intended use" regulation, which provides the basis for determining whether a product is regulated by the FDA and to what nature and extent. See 80 Fed. Reg. 57756 (September 25, 2015). The original rule contained a sentence that required manufacturers with any knowledge of off-label use of their products to provide adequate labeling for such use:

> But if a manufacturer knows, or has knowledge of facts that would give him notice, that a [drug or device] introduced into interstate commerce . . . is to be used for conditions, purposes, or uses other than the ones for which he offers it, *he is required to provide adequate labeling for such a drug/device which accords with such other uses to which the article is to be put.*
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> See 21 C.F.R. §§ 201.128 and 801.4 (emphasis added).

The proposed changes to the rule would have removed the "knowledge" sentence from the "intended use" definition, indicating that a company would not be subject to liability for having knowledge of unapproved uses of its products. The preamble to the proposal states that the FDA "would not regard a firm as intending an unapproved new use for an approved or cleared medical product based solely on the firm's knowledge that such product was being prescribed or used by doctors for such use." *See* 80 Fed. Reg. 57756 (September 25, 2015), at 57757. Removing the "knowledge" sentence, the FDA stated, would be done in an effort "to better reflect FDA's interpretation and application of these revisions." *Id.* at 57761.

The Final Rule

On January 9, 2017, the FDA released a different final version of the rule, which kept the "knowledge" sentence, and added a "totality of the evidence" standard:

> And if the *totality of the evidence* establishes that a manufacturer objectively intends that a device [or drug] introduced into interstate commerce by him is to be used for conditions, purposes, or uses other than ones for which it has been approved, cleared, granted marketing authorization, or is exempt from premarket notification requirements (if any), he is required, in accordance with section 502(f) of the Federal Food, Drug, and Cosmetic Act, or, as applicable, duly promulgated regulations exempting the device from the requirements of section 502(f)(1), to provide for such device [or drug] adequate labeling that accords with such other intended uses.
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> *See* 82 Fed. Reg. at 2217 (emphasis added).

The rule would require manufacturers to add labeling for unapproved uses known to the manufacturer, and also add labeling if a manufacturer intends, based on a "totality of the evidence," to promote a medical product for an unapproved use. The day the final rule was scheduled to take effect, February 8, 2017, pharmaceutical industry groups, including the Medical Information Working Group (MIWG), the Pharmaceutical Research and Manufacturers of America (PhRMA), and the Biotechnology Innovation Organization (BIO), filed a Petition asking for a stay and reconsideration.

The Petition

The industry groups' arguments can be condensed to three key issues. First, they argue the final rule violates the notice-and-comment provisions of the Administrative Procedure Act (APA), which requires new regulations be released for public comment prior to enactment. See Petition, at 11. The industry groups state that the APA requires the FDA to "make its views known to the public in a concrete and focused form so as to make criticism or formulation of alternatives possible." *HBO, Inc. v. FCC*, 567 F.2d 9, 36 (D.C. Cir. 1977). Specifically, the industry groups assert that the FDA must "describe the range of alternatives being considered with reasonable specificity," *Small Refiner Lead Phase-Down Task Force v. EPA*, 705 F.2d 506, 549 (D.C. Cir. 1983), "and set out [the agency's] thinking" so that parties be permitted to respond with an "adversarial critique of the agency," *HBO*, 567 F.2d at 36, 55.

Second, the industry groups argue that a "totality of the evidence" standard raises significant First Amendment and Fifth Amendment due process concerns. The

Petition states that the rule is "vague" because it allows for prosecution of misbranding violations based on interferences of promotional claims drawn from a "totality of circumstances" standard, which violates the constitution by failing to provide the parties "fair notice of conduct that is forbidden or required." *FCC v. Fox Television Stations, Inc.*, 132 S. Ct. 2307, 2317 (2012). See Petition, at 20.

Finally, the industry groups state that the rule would negatively impact public health by chilling valuable scientific speech. For example, the Petition asserts that "if a company engages in scientific exchange about off-label use, forecasts on and off-label uses, and scales production to meet the combined demands, a prosecutor could decide that this evidence reflects an off-label intended use." *Id.* at 21.

The one-year extension also allows the FDA and industry groups to further assess recent comments by the agency regarding First Amendment communications. In January 2017, the FDA released a memorandum entitled "Public Health Interests and First Amendment Considerations Related to Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products." The memorandum was issued to provide "additional background" in response to concerns that the agency failed to address the First Amendment in its public hearing notice. See January 2017 Public Health Memorandum, at 1. For example, the FDA reiterated its commitment to the development of "robust scientific data," while also "maintaining the premarket review process for safety and efficacy. . .". *Id.* at 4-5. The agency also cites to United States Supreme Court precedent in support of its position that restrictions on off-label promotions advance substantial government interests, and are therefore constitutional. *Id.* at 23.

FDA Response

On March 17, 2017, the FDA issued a clarification notice that the agency is extending the effective date of the rule change for one year, from March 21, 2017 to March 19, 2018. See Notice, at 1. The FDA states in the notice that the proposed amendments to the intended use regulations "were not intended to reflect a change in FDA's approach," and that in determining a product's intended use, it is the agency's "longstanding position" that they "may look at any relevant evidence." *Id.* at 5. The FDA further states that "good cause" exists for the delay, and that the agency is "seeking input on some specific questions and is also interested in any other pertinent information or comments stakeholders would like to provide regarding any aspect of the final rule…". *Id.*

The FDA is requesting comments on the following questions:

1. How should FDA consider situations such as those described in the announcement where companies and individuals distribute medical products and/or seek to import medical products without explicit promotional claims as FDA evaluates whether to adopt any of petitioners' suggested approaches to determining intended use?

2. What are the potential public health consequences, positive and negative, that should be considered in evaluating whether to adopt any of petitioners' suggested approaches to determining intended use? What other policy considerations are relevant when assessing approaches to intended use?

3. To the extent that your comment cites to First Amendment considerations as the legal rationale underlying your recommendations, how (if at all) do those considerations apply to the use of non-speech evidence in determining intended use, such as the circumstances surrounding the distribution of a product or the context in which it is sold?

4. In light of the petitioners' concerns about the language in the Final Rule, do stakeholders believe there is a distinction between considering "any relevant source of evidence" and "the totality of evidence"? Do stakeholders have suggestions about what wording provides the most clarity to regulated entities?

   Id. at 14-15.

Interested parties may submit comments on the docket here, by April 19, 2017. Enactment of the final rule has been officially extended to March 19, 2018, but until then, as comments are submitted and assessed, the conversation continues.

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Pharma and Life Sciences Industry Group

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