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Client Alert Commentary

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FDA Finalizes Guidance on Communications of Scientific Information on Unapproved Uses

The final guidance describes FDA's enforcement discretion policy for sharing scientific information on unapproved uses of approved products and suggests a safe harbor for sharing off-label information consistent with the guidance's recommendations.

Last week, amid an extraordinary release of 26 guidance documents on a single day, the Food and Drug Administration (FDA) published the highly anticipated final version of its "Communications From Firms to Health Care Providers Regarding Scientific Information on Unapproved Uses of Approved/ Cleared Medical Products: Questions and Answers" guidance document.[1] This final guidance revises the October 2023 draft guidance of the same name,[2] which itself revised and replaced FDA's 2014 guidance covering similar issues.[3]

The final guidance outlines FDA's views on when firms may, on their own initiative, communicate scientific information to healthcare providers (HCPs) regarding unapproved uses of their approved/ cleared medical products, or "SIUU communications."[4] Per the guidance, if a firm makes SIUU communications consistent with the guidance's recommendations, FDA does not intend to treat such communications — standing alone — as evidence of a new intended use.[5]

Key Takeaways

Below are key takeaways from the final guidance:

- **SIUU communications based on early-stage data may qualify for the enforcement discretion policy.** In the draft guidance, FDA generalized that data from early-stage product development "are unlikely to be sufficiently reliable by themselves to allow for a determination of clinical relevance."[6] On this basis, FDA asserted that SIUU communications based on early-stage data likely would fall outside the scope of the enforcement discretion policy.[7] The final guidance abandons this sweeping generalization and provides more flexibility for firms to make SIUU communications based on early-stage data if the data are from "scientifically sound" studies.[8]

- **SIUU communications should make source publications accessible to the communication's audience.** In the draft guidance, FDA recommended that firms describe key aspects of the communication's source material that may not be included in the communication itself (including all material aspects of and limitations related to study design,

methodology, and results), any conclusions from other relevant studies that are contrary to or cast doubt on the results shared, and citations for any such studies.[9] The final guidance permits firms to include such information in descriptive format but also adopts a blanket recommendation favoring industry-wide transparency: Firms should provide the source material as part of the firm-generated communication.[10]

- **Firm-generated communications may be based on source publications beyond reprints.** In the draft guidance, FDA's recommendations were specifically limited to firm-generated communications based on reprints, which FDA defines as copies of an article originally published by a medical or scientific journal.[11] The final guidance clarifies that firms can also prepare communications based on other types of source publications, including clinical resources (e.g., medical reference texts and clinical practice guidelines).[12]

- **Firm-generated communications may use presentational elements to explain or illustrate scientific content.** The final guidance states that firms may use presentational elements and other communication techniques to help explain or illustrate scientific content in an accurate way.[13] This is a welcome clarification to address concerns that FDA may have viewed the use of colors, typefaces, tables, charts, and more as inherently promotional in nature.

- **FDA discards the "clinically relevant" standard in favor of a focus on source publications that are scientifically sound.** In the draft guidance, FDA took the position that the studies or analyses described in source publications should be both scientifically sound and "clinically relevant," and defined "clinical relevance" as "provid[ing] information that is relevant to *HCPs* engaged in making clinical practice decisions for the care of an individual patient."[14] The final guidance discards this ambiguous standard and clarifies that source publications should describe studies and analyses that are scientifically sound (i.e., they meet generally accepted design and other methodological standards for the particular type of study or analysis performed).[15]

- **Certain communication techniques are categorically excluded from the enforcement discretion policy.** Although FDA abandoned its recommendation that SIUU communications not use "persuasive marketing techniques,"[16] FDA did not extend the enforcement discretion policy to SIUU communications that use communication techniques based on elements other than the communication's substance.[17] According to FDA, such techniques include celebrity endorsements, emotional appeals unrelated to the scientific content, gifts, promotional tag lines, jingles, and premium offers.[18]

- **A "call to value" may bring a firm-generated presentation outside of the enforcement discretion policy's scope.** The final guidance introduces the term "call to value," which refers to a communication technique that includes both a call to action and a value proposition that tells the audience how this action may benefit them.[19] A call to value that pre-judges the benefits of a medical product — e.g., "Click here to start improving your patients' lives today" — is outside the scope of the enforcement discretion policy.[20] But FDA clarified that calls to value that do not pre-judge a product's benefits — e.g., calls to value that invite an HCP to access a full article or read more about new data — do not by themselves disqualify an SIUU communication from the enforcement discretion policy's scope.[21]

- **Firms have an obligation to stay current with existing scientific knowledge.** The final guidance emphasizes that firms should take existing scientific knowledge into account when determining whether a source publication is appropriate to inform an SIUU communication.[22]

FDA makes clear that a firm should not rely on a source publication in bad faith if they know its conclusions have been refuted or that it was initially informed by a long-held misunderstanding later corrected in the scientific community.[23] Firms must also keep up with existing scientific knowledge to retract SIUU communications based initially on source publications that have later become inconsistent with existing scientific knowledge.[24]

- **The final guidance generally heightens a firm's obligations to vet source publications.** In addition to the new policy on existing scientific knowledge, the final guidance includes several new recommendations that collectively impose a greater burden on firms to vet source publications. To meet the scientifically sound standard, the final guidance states that any study or analysis should be evaluated in light of its limitations.[25] Source publications should be evaluated for statistical rigor.[26] And clinical practice guides should be vetted to ensure they do not misrepresent or overstate findings from a study or analysis.[27]

For a life sciences industry all too familiar with FDA's historically restrictive — and unconstitutional — approach to communications regarding unapproved uses, the guidance is a milestone in FDA's evolving approach toward "off-label promotion." Building off the progress of the draft guidance, the final guidance vindicates the First Amendment rights of medical product companies by recognizing that they may, under certain conditions, proactively make SIUU communications. That said, FDA continues to take a restrictive view on when an SIUU communication does not serve as evidence of a new intended use by placing significant restrictions on the sources and permissible content in such communications. As explained below, the final guidance also leaves open several questions.

FDA's Prior Regulation of Off-Label Information

To the benefit of medical product companies, FDA's effort to regulate SIUU communications has significantly evolved since the early 2000s. As industry observers likely know, throughout the 2000s, the Department of Justice (DOJ) and FDA frequently pursued enforcement actions against medical product companies for so-called off-label communications. The foundation for many of these enforcement actions was evidence of how sales representatives promoted medical products to HCPs.

Against this backdrop, Congress and the courts began to recognize that medical product companies have a First Amendment right to disseminate off-label information under certain circumstances. In 1997, as part of the FDA Modernization Act of 1997 (FDAMA), Congress amended the Federal Food, Drug, and Cosmetic Act (FDCA) to explicitly specify the circumstances under which medical product companies could legally disseminate medical and scientific information discussing unapproved uses of approved drugs and cleared or approved medical devices to HCPs.[28] FDA subsequently implemented regulations specifying the kind of information medical product companies could disseminate and the detailed procedures medical product companies were required to follow before disseminating information on an unapproved use of an approved product.[29]

But FDAMA and FDA's regulations were quickly challenged and held unconstitutional by a district court.[30] On appeal, the D.C. Circuit vacated the district court's decision based on FDA's clarification that FDAMA and its implementing regulations provided FDA with no independent authority to proscribe speech.[31] FDA explained that, as long as medical product companies followed FDAMA's provisions and implementing regulations for disseminating off-label information, they would be protected under the statutory and regulatory "safe harbor."[32] FDA then published a notice in the Federal Register clarifying that FDAMA and its regulations constituted this safe harbor for medical product companies that comply with them.[33] FDAMA's provisions lapsed in 2006, and FDA's implementing regulations then became inapplicable.[34]

In 2009, in an effort to provide industry with more insight after FDAMA's provisions lapsed, FDA published a guidance document providing its views on the dissemination of reprints.[35] Meanwhile, FDA and DOJ continued to pursue an aggressive enforcement agenda against medical product companies for off-label communications. But after the US Court of Appeals for the Second Circuit issued its decision in *U.S. v. Caronia*,[36] the tides began to shift in favor of the life sciences industry. In *Caronia*, the court construed the FDCA's misbranding provisions "as not prohibiting and criminalizing the truthful off-label promotion of FDA-approved prescription drugs."[37] The court concluded that "the government cannot prosecute pharmaceutical manufacturers and their representatives under the FDCA for speech promoting the lawful, off-label use of an FDA-approved drug."[38]

In another significant win for medical product companies, the court in *Amarin Pharma Inc. v. FDA* held that "[w]here the speech at issue consists of truthful and non-misleading speech promoting the off-label use of an FDA-approved drug, such speech, under *Caronia*, *cannot* be the act upon which an action for misbranding is based."[39] The *Amarin* court rejected FDA's argument that it could bring a misbranding action against Amarin based on statements reporting the results of a study on an unapproved use of Amarin's drug.[40] Under *Caronia*, the *Amarin* court reasoned, FDA may *not* bring such an action based on truthful promotional speech alone."[41]

After *Caronia* and *Amarin,* enforcement actions against medical product companies began to focus less on off-label promotion, and fewer of DOJ's enforcement actions included a criminal component. Meanwhile, FDA issued a 2014 draft guidance in its ongoing effort to consider, develop, and refine its policies and recommendations relating to communications from firms to HCPs regarding scientific information on unapproved uses of the firms' approved or cleared medical products.[42] The draft guidance, titled "Distributing Scientific and Medical Publications on Unapproved New Uses – Recommended Practices," further explained FDA's policies and included FDA's recommendations on a firm's dissemination of scientific or medical reference texts.[43]

FDA's October 2023 draft guidance superseded the nearly decade-old draft guidance.[44] Although not without significant limitations, the October 2023 draft guidance was the strongest signal FDA had sent to date recognizing medical product companies' First Amendment right to proactively disseminate certain truthful and non-misleading information regarding unapproved uses of approved products. The January 2025 final guidance lifts some of the arbitrary constraints imposed in the October 2023 draft guidance and thus represents another milestone in the evolution of FDA's views on off-label communications and scientific information to HCPs regarding unapproved uses.

Remaining Uncertainties

As summarized above, the final guidance provides important clarification on a number of questions raised by the draft guidance. Nevertheless, the final guidance leaves industry to grapple with open questions about how FDA will implement it. Below, we identify a few of these open questions:

- FDA is clear that the use of certain communication techniques, such as celebrity endorsements or emotional appeals unrelated to scientific content, will bring an SIUU communication outside the enforcement discretion policy's scope.[45] It remains to be seen whether FDA will view the use of additional communication techniques as attempts to influence decisions based on elements other than the communication's substance. For example, FDA could assert that asking a prominent patient advocate to share the results of a recent study about an unapproved use of a firm's approved drug is a communication technique that renders the communication ineligible for the enforcement discretion policy.

- The final guidance advises firms to consider whether existing scientific knowledge has refuted a conclusion from a study described in the source publication supporting a particular communication.[46] According to FDA, the act of disseminating a communication based on a source publication that describes such a study would not fall within the guidance's enforcement discretion policy.[47] But the guidance does not offer additional clarification into what qualifies as "existing scientific knowledge," or what firms should do if they disagree in good faith with existing scientific knowledge about the study at hand.

- As with the draft guidance, the final guidance acknowledges that firms share SIUU communications through different media, and that FDA's recommendations apply regardless of the medium of communication.[48]However, in the final guidance, FDA clarifies that firms should not use platforms with character-space limitations to host an SIUU communication; instead, firms may use such platforms to direct an HCP to an SIUU communication without naming the product.[49] Aside from potentially excessive commercial speech restrictions — First Amendment protections presumably would extend to a firm's ability to name the product itself even in a platform with character-space limitations — FDA's recommendation fails to offer clarity on the kinds of platforms that are character-space limited and how a firm could disseminate an SIUU communication via such platform that would fall under FDA's enforcement discretion policy. For example, it is not clear whether a firm-generated presentation shared on an Instagram page with all the necessary disclaimers in the caption of the post would be inconsistent with the final guidance's recommendations.

- The final guidance has not yet been cleared by the White House's Office of Information and Regulatory Affairs (OIRA).[50] It is not clear why FDA released the guidance without OIRA's sign-off, but the situation is not common.

Latham & Watkins will continue to monitor developments in this space.

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Endnotes

[1] FDA, Communications From Firms to Health Care Providers Regarding Scientific Information on Unapproved Uses of Approved/Cleared Medical Products: Questions and Answers, Guidance for Industry (Jan. 2025), https://www.fda.gov/media/184871/download (January 2025 Final Guidance).

[2] Latham & Watkins podcast: Has FDA Meaningfully Changed Its Restrictions on Off-Label Communications? (Dec. 13, 2023).

[3] FDA, Communications From Firms to Health Care Providers Regarding Scientific Information on Unapproved Uses of Approved/Cleared Medical Products: Questions and Answers, Draft Guidance for Industry (Oct. 2023), at 3-4 (October 2023 Draft Guidance).

[4] January 2025 Final Guidance at 6.

[5] *Id.* at 1.

[6] October 2023 Draft Guidance at 12.

[7] *Id.*

[8] January 2025 Final Guidance at 12.

[9] October 2023 Draft Guidance at 14.

[10] January 2025 Final Guidance at 25.

[11] October 2023 Draft Guidance at 20, 25.

[12] January 2025 Final Guidance at 25 ("The firm-generated presentation should be limited to the scientific information on unapproved use(s) from one or more source publications, and the source publication(s) should be consistent with the recommendations in Q1 and Q4 of this guidance.").

[13] January 2025 Final Guidance at 26.

[14] October 2023 Draft Guidance at 2.

[15] January 2025 Final Guidance at 12.

[16] October 2023 Draft Guidance at 15.

[17] January 2025 Final Guidance at 27.

[18] *Id.*

[19] January 2025 Final Guidance at 27 n.64.

[20] *Id.* at 27-28.

[21] *Id.*

[22] *Id.* at 13.

[23] *Id.* at 14.

[24] *Id.* at 14-15.

[25] *Id.* at 12.

[26] *Id.* at 12.

[27] *Id.* at 22-23.

[28] Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2358, §§ 551-553, 111 Stat. 2356-2359 (1997).

[29] *Id.*

[30] *Washington Legal Foundation v. Henney*, 56 F.Supp. 2d 81, 89; Order Granting Summary Judgment and Permanent Injunction, 64 Fed. Reg. 44025 (Aug. 12, 1999).

[31] *Washington Legal Foundation v. Henney*, 202 F.3d 331, 332 (D.C. Cir. 2000).

[32] *Id.* at 336; Decision in Washington Legal Foundation v. Henney, 65 Fed. Reg. 14286, 14287 (Mar. 16, 2020).

[33] 65 Fed. Reg. 14287.

[34] FDA, Good Reprint Practices for the Distribution of Medical Journal Articles and Medical or Scientific Reference Publications on Unapproved New Uses of Approved Drugs and Approved or Cleared Medical Devices (Jan. 2009), at 2.

[35] *Id.*

[36] *U.S. v. Caronia*, 703 F.3d 149 (2d Cir. 2012).

[37] *Id.* at 168-169.

[38] *Id.* at 169.

[39] *Amarin Pharma, Inc. v. U.S. Food & Drug Admin.,* 119 F.Supp 3d 196, 226 (S.D.N.Y. 2015).

[40] *Id.* at 224.

[41] *Id.* at 226.

[42] January 2025 Final Guidance at 9.

[43] FDA, Distributing Scientific and Medical Publications on Risk Information for Approved Prescription Drugs and Biological Products—Recommended Practices (June 2014), at 1-2, https://www.fda.gov/media/88674/download.

[44] October 2023 Draft Guidance at 4.

[45] January 2025 Final Guidance at 26-27.

[46] *Id.* at 13-14.

[47] *Id.*

[48] October 2023 Draft Guidance at 6; January 2025 Final Guidance at 2 n.4.

[49] January 2025 Final Guidance at 20.

[50] Communications From Firms to Health Care Providers Regarding Scientific Information on Unapproved Uses of Approved/Cleared Medical Products: Questions and Answers; Guidance for Industry; Availability; Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request, 90 Fed. Reg. 1146 (Jan. 7, 2025).