Articles + Publications | January 22, 2025

FDA Finalizes Guidance on Communications Regarding Unapproved Uses of Medical Products

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On January 7, the U.S. Food and Drug Administration (FDA) finalized its October 2023 guidance document titled "Communications From Firms to Health Care Providers Regarding Scientific Information on Unapproved Uses of Approved/Cleared Medical Products" (the final guidance). This guidance finalizes the draft issued in October 2023, and while most of the concepts from the initial draft remain, the final guidance contains several important changes resulting from stakeholder comments (for more information regarding the draft guidance, please see our 2023 client alert). The final guidance is open for comment through February 21, and is not for current implementation, pending the Office of Management and Budget's (OMB) review of collected information.

The final guidance conveys the FDA's enforcement policy regarding the use of scientific information on unapproved uses (SIUU) of approved/cleared medical products in communications with health care providers (HCPs). The FDA notes that it is issuing this final guidance to "provide reassurance to firms that, if they choose to provide communications consistent with the recommendations" in the guidance document, the FDA will not use that communication, "standing alone, as evidence of a new intended use."

Consistent with prior guidance documents, the FDA makes clear it is paramount that an SIUU communication be truthful and non-misleading, and that it should "provide and appropriately present all information necessary for HCPs to understand and evaluate the strengths and weaknesses, validity, and clinical utility of the scientific information." The guidance also distinguishes between SIUU firm-generated presentations and source publications. Source publications, as referenced in the guidance, include scientific or medical publications generally available from independent publishers. Source publications serve as the basis for SIUU communications. These materials such as peer-reviewed journal articles, clinical practice guidelines, or reference texts provide foundational information and are expected to meet rigorous standards of scientific validity to ensure their reliability when informing clinical decisions. In contrast, firm-generated presentations refer to materials created by a firm that summarize or analyze source publications, often tailored for dissemination to HCPs alongside the original source publications.

What Changed Since 2023

The October 2023 draft guidance expanded on the FDA's earlier stance regarding the dissemination of scientific and medical publications, allowing firms to proactively share "firm-generated presentations of scientific information" alongside source publications. The 2023 draft guidance required these source publications to be "scientifically sound and clinically relevant." In the draft guidance, the FDA clarified: "To be clinically relevant, the studies or analyses, in addition to being scientifically sound, should provide information that is pertinent to HCPs

engaged in making clinical practice decisions for the care of an individual patient."

While the final guidance removed the explicit term "clinically relevant," it introduced a stricter standard by requiring that SIUU communication be "scientifically sound" and not "likely to lead to direct or indirect patient harm when HCPs rely upon the communication to inform clinical decisions." This represents a shift from clinical relevance to a focus on preventing harm through scientific soundness based on generally accepted scientific principles for design and methodology. For example, the FDA indicates that direct harm might occur if a source publication recommends a medical product for a population known to experience adverse effects from its use (such as the risk of severe birth defects when a drug is used by pregnant women). Indirect harm, on the other hand, could result from misleading information causing HCPs to prescribe an ineffective treatment, depriving patients of critical opportunities for effective care. The final guidance also emphasizes that firms should account for "existing scientific knowledge" in determining whether source publications are appropriate for inclusion in an SIUU communication and whether such knowledge refutes the source publication's conclusion or corrects a long-held misunderstanding. Notably, the FDA has replaced the statement that real-world data and evidence can be scientifically sound and clinically relevant to simply point readers, in a footnote, to its prior thinking on real-world data and evidence.

The final guidance further provides additional context to the requirement that communications be both "truthful and non-misleading," explaining that a firm-generated presentation should (1) be limited to scientific information on unapproved use(s) from appropriate source publication(s); (2) include the source publication(s); (3) provide all material information necessary to interpret any represented study results (*e.g.*, relevant design, methodology, and limitations); and (4) include clear disclosures indicating it is firm-generated (*e.g.*, 'This presentation was developed by FIRM X') and clearly identify which portions are firm-generated. It also specifies that a firm-generated presentation should not (1) imply broader or more-general experience with the product than is supported by the source publication; (2) include representations about safety or effectiveness for unapproved use(s) that are not consistent with the source publication; (3) present conclusions on safety or effectiveness without attribution to the source publication and immediate disclosure of any relevant author or contributor relationships; (4) present information from the source publication out of context; (5) use statistical methods or techniques not supported by the data to suggest clinical significance or validity; or (6) employ textual or graphic elements that obscure or distort the scientific content. A truthful, non-misleading presentation "should provide and appropriately present all information necessary for HCPs to understand and evaluate the strengths and weaknesses, validity, and clinical utility of the presented scientific information on unapproved use(s)."

The final guidance also more directly addresses "persuasive marketing techniques" used by firms, a term that was not well-defined and the focus of industry feedback on the draft guidance, moving away from the term entirely to instead provide specific examples of correct and incorrect communications. Examples include:

- At gatherings like medical or scientific conferences, "where programming is not selected and determined by the conference organizers," SIUU communications should be clearly and prominently identified and separated from promotional guidance. The FDA specifically recommends use of a separate space in a conference booth "where SIUU communications can be shared, separate from the booth space where promotional communications about approved uses are shared."

- Where firms share information about both approved and unapproved uses on websites, SIUU communications

should be on a distinct web page from any page displaying promotional communications and be clearly identified. The firm's site should not link between the promotional and SIUU webpages.

- Where firms share information about both approved and unapproved uses via email, those sharing SIUU communications should be separate from those sharing promotional communications and be clearly identified.

- If SIUU communications are shared in-person between a firm and HCP, the SIUU communications should be separate from any promotional communications about approved uses and "not attached to or intermingled with" those promotional communications.

The FDA explains that any communication appearing promotional or attempting to persuade rather than inform would not fall under the guidance's protections. While both the draft and final guidance state that "SIUU communications should be separate from promotional communications about approved uses of medical products," the final guidance illustrates this separation with four examples — covering conferences, websites, emails, and in-person visits with HCPs. Of note, it provides explicit examples of permissible and impermissible communications, emphasizing the avoidance of promotional taglines, emotional appeals, and imagery designed to elicit nonscientific responses. It recommends presenting scientific information clearly and distinctly from promotional content, with appropriate disclosures to ensure health care providers can interpret the information accurately.

Additionally, the final guidance introduces "calls to value," a concept absent from the 2023 draft. It distinguishes statements like "Click here to start improving your patients' lives today," which pre-judge a product's benefits, from statements such as "Read now to learn more about this new data on medical product X," which do not. The final guidance concludes by explaining the importance of presenting communications "in a manner that is unlikely to lead HCPs to base those decisions on conclusions about the safety and effectiveness of the unapproved use that are not in alignment with or that go beyond what is justified by the underlying scientific information."

Key Takeaways

In short, the final guidance reflects the latest evolution of the FDA's planned enforcement for SIUU communications, which opens up potential new opportunities for proactive communications of scientifically sound, truthful, non-misleading and non-promotional off-label information. If manufacturers have questions about the impact of the final guidance on their SIUU communications, we recommend consulting with legal counsel, including Troutman Pepper Locke.

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