New Year, New Recommendations: FDA Finalizes SIUU Guidance

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On January 6, 2025, the FDA issued final guidance (subject to implementation by the Office of Management and Budget) for off-label communications about approved products entitled, ***Communications From Firms to Health Care Providers Regarding Scientific Information on Unapproved Uses of Approved/Cleared Medical Products: Questions and Answers*** (Final Guidance), reorganizing and revising its draft guidance of the same title from October 2023 (Draft Guidance). We discussed the Draft Guidance in a previous update. This Client Alert discusses the Final Guidance which includes some notable changes from the Draft Guidance and important takeaways as companies begin to implement initiatives that incorporate scientific information pertaining to new uses not approved by the FDA.

The Final Guidance describes the FDA's enforcement policy related to certain firm-initiated communications of scientific information about unapproved uses of approved/cleared medical products (SIUU). A "firm" is defined to include entities such as a manufacturer or one legally responsible for labeling products and anyone communicating on their behalf. "SIUU communications" are defined as firm-initiated communications of scientific information on unapproved use(s) of the firm's approved/cleared medical product that (i) are shared with health care providers involved in prescribing or administering approved/cleared medical products to individual patients (HCPs); (ii) include recommended disclosures from the Final Guidance; and (iii) include one or more of the following source publications: published reprints, or published clinical resources (clinical practice guidelines (CPGs), reference texts, and materials from digital clinical practice resources). SIUU communications can also include firm-*generated* presentations. The Final Guidance reassures firms that if they provide communications consistent with the Final Guidance, the agency "does not intend to use the firm's dissemination of such communication *standing alone* as evidence of a new intended use" (emphasis added).

Specifically, its recommendations are centered around the principles that SIUU communications be "truthful and non-misleading" and "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 on unapproved use(s) in the SIUU communication." In doing so, the Final Guidance states such communications must maintain a "careful balance" between supporting an HCP's interest in SIUU for the care and management of individual patients while not undermining other government interests including premarket requirements that advance public health and safety.

Although these principles are stated similarly in the Draft Guidance, after receiving stakeholder comments that it was ambiguous and fraught with Constitutional concerns, the FDA reorganized the guiding principles regarding SIUU and incorporated various revisions into the Final Guidance, some of which we will discuss below.

Appropriateness of Source Publications in SIUU Communications

Regarding what firms should consider when determining whether a source publication should be included in a SIUU communication, the FDA makes the following recommendations:

- Source publications included in SIUU communications should describe studies and analyses that are "scientifically sound," meeting accepted design and methodological standards for the particular type of study or analysis performed and evaluated in view of limitations
- Firms should take existing scientific knowledge into account when preparing and disseminating the communication
- Conclusions should align with the prespecified hypothesis or research question and be supported by results from the study or analysis

The Draft Guidance repeatedly stated that SIUU communications should describe studies or analyses that are "scientifically sound and provide clinically relevant information." Presumably, in response to comments from the industry, the Final Guidance removed the wording "clinically relevant" and, as noted above, reiterated the importance that SIUU communications provide *all information necessary* for HCPs to understand and evaluate scientific information.

The Final Guidance includes a lengthy list of disclosures and other information that firms should include as part of their SIUU communications, reflecting the list contained in the Draft Guidance plus some additional details. The recommended disclosures include, for example: (i) a statement that the unapproved use(s) of the product has not been approved and that the safety and effectiveness of the product for such use(s) has not been established; (ii) a statement disclosing the approved use(s) of the medical product, including any limitations of use, and a copy of the label (or a mechanism for obtaining it); (iii) a statement describing any serious, life-threatening, or fatal risks posed by the product that are known or in the label and relevant to the unapproved use(s) as well as any established risk evaluation and mitigation strategy or REMS; (iv) a statement identifying any authors, editors, or other contributors to publication(s) included in the SIUU communication who were employees, consultants, or received compensation from the firm for writing, editing, or contributing to the publication; and (v) a description of material information and other conclusions, as applicable and to the extent not described in the source publication(s).

Presentational Considerations

The Final Guidance provides "presentational considerations" that firms should take into account, beginning with the premise that the recommended disclosures should be "clearly and prominently" presented. The Final Guidance also maintains that all SIUU communications should be separate from promotional communications regarding approved uses of medical products and only shared through media/platforms that allow for the implementation of the recommendations from the Final Guidance. Additionally, the FDA recommends that firms ensure that personnel that share SIUU communications have specialized training in providing such communications.

Notably, the Final Guidance removes the Draft Guidance's recommendations that: (i) SIUU communications not use "persuasive marketing techniques" and (ii) firms use "plain language" in the content they develop for SIUU communications. Despite the removal of these specific phrases, the Final Guidance retains principles that appear to address these matters more broadly. For example, as for the removal of the plain language recommendation, the Final Guidance still contains the policy statement that these communications should present all information necessary for HCPs to understand and evaluate the scientific information. With respect to the removal of the "persuasive marketing techniques" language, as noted above, the FDA retained its recommendation that SIUU communications be separate from promotional communications and also says that techniques that encourage the use of the product based on elements *other than* the communication's scientific content are outside the scope of the Final Guidance.

Additional Recommendations

New in the Final Guidance, the FDA points out that firm-generated presentations can be distinguished from other types of SIUU communications. In making this point, the FDA states that companies are the ones creating such presentations, which

are not generally available in the way that source publications are, and thus lack "the same level of independence in their development and publication as source publications that meet the recommendations set forth in [the Final Guidance]."

The FDA reiterates that these presentations should be consistent with other aspects of the Final Guidance, *i.e.* they must be truthful and non-misleading, as well as provide and appropriately present all information necessary for HCPs to understand and evaluate scientific information on unapproved use(s). The Final Guidance provides several "dos" and "don'ts" for firm-generated presentations and also clarifies an ambiguity to indicate that the recommendations apply to firm-generated presentations of scientific information from any of the source publications mentioned in the Final Guidance, *i.e.* reprints, CPGs, reference texts and materials from digital clinical practice resources, as the Draft Guidance only mentioned reprints in connection with firm-generated presentations. These include that firms may not:

- Imply that the study, analysis, or underlying data from the source presentation represents a larger or more general experience with the product than it actually does;
- Include representations or suggestions about the safety or effectiveness of the product for the unapproved use(s) that are not consistent with the source publication;
- Present conclusions or representations about the safety or effectiveness of the unapproved uses(s) without attributing such statement expressly to the source publication and without following it with a statement identifying authors, editors, or contributors who were employed or received compensation from the company at the time of writing, editing or contributing to the source publication;
- Present information, *e.g.* quotes, excerpts, paraphrases, and conclusions, from the source publication out of context;
- Use presentational elements to obscure or distort the scientific content; or
- Use statistical analyses or techniques to indicate the clinical significance or validity of a finding not supported by the data in the source publication.

Notwithstanding these suggestions, the Final Guidance makes it clear that firms may use presentational elements and other communication techniques to help explain or illustrate scientific content in an accurate way or to help ensure clear and prominent presentation of the recommended disclosures.

It is in this section that the FDA states that the enforcement policy within the Final Guidance does not apply to communication techniques that encourage the unapproved use of an approved product based on information *other than* scientific content, such as celebrity endorsements, emotional appeals unrelated to scientific content, gifts, promotional tag lines, jingles, and premium offers. In addition, the Final Guidance states that "calls to value," *i.e.* suggestions that pre-judge the benefit(s) of a medical product for individual patients, are likewise outside the scope of the Final Guidance. The FDA states that these types of firm-generated presentations suggest an effort to convince HCPs to prescribe or use the product for the unapproved use, in contrast to providing the HCP with scientific information so he or she can evaluate and make their own clinical decisions. To that end, the Final Guidance states that "[w]ithout this boundary regarding communication techniques in firm-generated presentations, there would not be a meaningful distinction between firm-generated presentations included in SIUU communications and promotional activities."

Conclusion

The FDA's issuance of the Final Guidance is an important step toward formalizing its policy on firm communication of SIUU to HCPs involved in prescribing or administering products to patients as part of its ongoing efforts regarding its recommendations about such communications. Companies should endeavor to implement such recommendations as SIUU communications are evaluated from a medical, legal, and regulatory compliance perspective.

Porzio's team of Life Sciences attorneys can assist companies in navigating the Final Guidance and its recommendations around scientific discussions and any potential promotional considerations, including those related to firm-generated presentations while assessing other associated laws and regulations.