Navigating the New FDA Draft Guidance: Evolving Manufacturer Considerations When Providing Scientific Information for Unapproved Uses

November 3, 2023

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Is your company providing scientific information related to an unapproved use for an approved or cleared drug or medical device? Are you ready for another acronym? Last week, FDA released an important update to its draft guidance regarding manufacturer communications to Health Care Providers (HCPs) about scientific information on unapproved use(s) of approved/cleared medical products (Guidance). The Guidance applies to information about both human and animal drugs, along with medical devices. Importantly, the Guidance does not apply to any communications about a medical product that is an "unapproved product."

Updating its 2014 draft guidance on the same topic- *Distributing Scientific and Medical Publications on Unapproved New Uses- Recommended Practices*, the new (albeit still draft) Guidance attempts to clarify FDA's thinking about these communications. It provides, among other things, "dos" and "don'ts" as well as suggested disclaimers for such communications for companies to consider when providing information related to an unapproved use for an approved product under the guise of "scientific discussion." The Guidance offers examples of statements to consider when providing these communications, keeping in mind the need to balance providing scientific information to HCPs to inform their clinical practice decisions with prevailing government interests. Notably, the Guidance has coined a new acronym to add to the industry's long list, *i.e.,* "scientific information on unapproved use(s)" will now be referred to as "SIUU." The method or mode of the SIUU communication is irrelevant, as the Guidance will apply regardless of how the information is conveyed to HCPs.

The Guidance applies to entities such as manufacturers or those legally responsible for labeling products (defined within the Guidance as a "Firm") and defines the "types of communications" that may be provided to HCPs such as: published scientific or medical journal articles (*i.e.,* reprints); published clinical reference resources, including clinical practice guidelines, scientific or medical references, reference texts, and materials from independent clinical practice resources; and firm-generated presentations of scientific information from an accompanying published reprint. In providing the Guidance, FDA has sought to balance the support for an HCP learning about unapproved use(s) of approved or cleared products to assist in appropriate prescribing decisions with the potential harm to patients that could result before safety and efficacy has been demonstrated for new uses. Greater detail can be found in the Guidance, which offers specific recommendations for companies to consider, depending on the proposed SIUU communication(s).

To help achieve this balance, the Guidance provides a framework based on certain foundational concepts:

1. SIUU communications should be truthful, non-misleading, factual, and unbiased, and provide all information necessary for HCPs to interpret the "strengths and weaknesses and validity and utility of the information in the SIUU communication."

2. Any study or analysis described in a source publication that serves as the basis for an SIUU communication should be scientifically sound and provide information that is clinically relevant to HCPs.

3. The manner of presentation of SIUU communications must be considered.

In the Guidance, FDA expands upon these foundational concepts with suggestions as to how to comply with its recommendations.

First, to ensure that an SIUU communication is truthful, non-misleading, factual, and unbiased, and provides all essential information for HCPs to interpret the strengths, weaknesses, and validity and utility of the information in the communication, the Guidance provides a list of (strongly) suggested disclaimers that includes: (i) a statement that the unapproved use of the product has not been approved by FDA and that the safety and effectiveness of the product has not been established; (ii) a statement disclosing the approved use(s) of the product that should include any limitations of use specified on the approved label; (iii) a statement disclosing any limitations, restrictions, cautions, or warnings as described on the approved label; (iv) a copy of the most recent approved label, or a mechanism for obtaining it; (v) any contraindications found on the approved label; (vi) a description of any life-threatening or fatal risks posed by the product found on the label or known to the company relevant to the unapproved use(s); (vii) a statement identifying any of the SIUU communication's known authors, editors, or contributors who are employees or compensated by the manufacturer at the time of the writing or editing of the communication; and (viii) the publication date of any referenced or included publication if such reference or publication is not specified in the communication.

In addition, if an SIUU communication is based on a source that is principally focused on a particular study/ies, the SIUU communication should include a description of all material aspects of the study/ies, material limitations related to such study/ies' design, methodology and results, and any conclusions for other relevant studies that may generate doubt or are contrary to the results of such study/ies, including citations.

Second, to be regarded as "scientifically sound," the Guidance suggests that any relied-upon studies or analyses should meet generally accepted design and other methodological requirements, considering established and existing scientific principles and knowledge. Further, to be considered "clinically relevant," the studies or analyses should provide information germane to HCPs that are making clinical practice decisions for individual patients. The Guidance specifically notes that real-world data and real-world evidence may be regarded as both scientifically sound and clinically relevant under certain circumstances, depending on the nature of the data and/or analyses. SIUU communications that distort studies, and those based on publications that distort studies, or rely on studies without an adequate control or comparison group to permit appropriate scientific evaluation, may not be considered appropriate under the Guidance and potentially violate certain FDA regulations.

Finally, the Guidance provides significant "presentational considerations" to equalize competing interests. These considerations include recommendations that support the concept that, in addition to being truthful and non-misleading, the SIUU communication is also factual and unbiased. Such recommendations include: (i) that all SIUU communications "clearly and prominently" present all of the recommended disclosures found in the Guidance; (ii) to avoid the appearance of inappropriately influencing the independence of an HCP's judgment, SIUU communications should not contain "persuasive marketing techniques,"[1] as FDA points out that such marketing techniques are "effective at influencing attitudes and behaviors" of HCPs; (iii) all SIUU communications must be separate and distinct from the company's promotional communications regarding approved use(s) to "reduce the risk of HCPs conflating the approved and unapproved use information"; (iv) SIUU communications should be shared through media (*e.g.*, paper or digital) and other

platforms that allow for the implementation of the recommendations found in the Guidance; and (v) to facilitate comprehension, companies should consider the use of “plain language” as they develop content for SIUU communications. This includes avoiding complicated acronyms or abbreviations as well as clearly explaining scientific and technical terms if such terms are used in the SIUU communication.

While some of the concepts embodied in the Guidance may not be novel, FDA appears to have clarified its thinking with respect to scientific discussions about approved or cleared products for new/unapproved uses. While the Guidance may be viewed as providing more latitude on the provision of these types of manufacturer communications, each SIUU communication should still be vetted for legal and regulatory considerations. The Guidance also demonstrates the value of an HCP's clinical practice while providing reminders of the importance of patient care and safety. Porzio's team of Life Sciences attorneys can assist companies in navigating FDA's recommendations around scientific discussions and any potential promotional considerations, including those related to firm-generated presentations, while assessing other associated laws and regulations.

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[1]These include, without limitation, celebrity endorsements, premium offers, and gifts.