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FDA Issues Draft Guidance, Requests Public Comments on Communication of Off-Label Information

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The U.S. Food and Drug Administration is evaluating its policies regarding the communication of off-label information for drugs, biologics and devices, with the issuance of a draft guidance and the opening of a docket for public comments. In this newsletter, the authors summarize the agency's draft guidance and request for public comments, and identify some key implications of these documents.

On December 27, 2011, the U.S. Food and Drug Administration (FDA) published a long-awaited draft guidance entitled Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices. The draft guidance, which is open for comment until March 29, 2012, is intended to clarify the agency's policies regarding the manner in which a manufacturer or distributor of an FDA-approved product may respond to an unsolicited request for information regarding off-label use(s).

Moreover, on December 28, 2011, the FDA published a notice in the *Federal Register* entitled Communications and Activities Related to Off-Label Uses of Marketed Products and Use of Products Not Yet Legally Marketed; Request for Information and Comments, in which it announced it had opened a new docket and invited public comment on issues related to communications regarding off-label use(s) of FDA-regulated products. In the notice, the FDA identifies issues, including 13 specific items, on which it would be interested in receiving comments. The agency will accept comments on these issues until March 27, 2012.

Summary of Draft Guidance

The draft guidance provides recommendations to manufacturers and distributors that would like to respond to *unsolicited* requests for information about off-label uses. Insofar as an entity responds to an unsolicited request for information about an off-label use in the manner described in the draft guidance, the FDA has indicated that it does not intend to use such responses as evidence of the firm's intent that a product be used off-label. (The U.S. Department of Justice is not, of course, bound by this guidance from the FDA.)

The guidance defines an "unsolicited request" as one initiated by a person or entity that is completely independent of the firm that responds to the request for information; a request that is prompted in any way by a manufacturer or its representatives is not an unsolicited request. The guidance document divides unsolicited requests between the nonpublic and public varieties. A nonpublic unsolicited request is an unsolicited request that is directed privately to an entity via one-on-one communication. Conversely, a public unsolicited request is an unsolicited request made in a

public forum, whether directed to an entity specifically or to a forum at large. The agency notes that there have been changes to communications brought about by the rise of social media and defines a public unsolicited request to include a request made via emerging electronic media, such as a product website, discussion board, chat room or other public electronic forum.

The FDA makes the following recommendations with respect to a company's response to a *nonpublic* unsolicited request for off-label information:

- The response should be provided only to the individual making the request.
- The response should be tailored only to answer the specific question(s) asked.
- The response should be truthful, non-misleading, accurate and balanced.
- The response should be scientific in nature.
- The response should be generated by medical or scientific personnel independent from the entity's sales or marketing department.

Additionally, the FDA recommends the response be accompanied by the following:

- A copy of the product's FDA-approved labeling
- A prominent statement notifying the recipient that the FDA has not approved or cleared the product as safe and effective for the use addressed in the materials provided
- A prominent statement disclosing the indication(s) for which the FDA has approved or cleared the product
- A prominent statement providing all important safety information including, if applicable, any boxed warning for the product
- A complete list of references for all of the information included in the response

Finally, the FDA recommends the manufacturer/distributor maintain records describing:

- The nature of the request for information
- The information provided to the requester
- Any follow-up inquiries or questions from the requestor

In considering how entities should respond to a public unsolicited request, the FDA expressed concern that entities may post, in a chat room for example, detailed online responses to questions about off-label uses in a manner that would make such information accessible to individuals who have not requested such information. The FDA also expressed concern that due to the enduring nature of online responses, specific information provided in response to such requests may become outdated. With these considerations in mind, the FDA makes the following recommendations for responses to *public* unsolicited requests for information about off-label uses:

- An entity should respond only when the request pertains specifically to its own named product (*i.e.*, the request is not solely about a competitor's product).
- The entity's public response should be limited to providing the firm's contact information and should not include any off-label information. Any substantive communication about off-label uses for the product that is provided in response to the original unsolicited off-label question, should occur solely between the firm and the individual who made the request.
- Representatives who provide public responses should clearly disclose their involvement with a particular firm.
- The response should not be promotional in nature or tone.

The FDA will accept comments and suggestions regarding this document until March 29, 2012.

Summary of Request for Comments

In its *Federal Register* notice, the FDA asked for public comments regarding communications and activities related to off-label uses of marketed products and use(s) of products that are not yet legally marketed. In the notice, the FDA indicated that it would be particularly interested in reviewing the public's response to a group of 13 questions. Representative questions from this group include:

- What types of activities fall under scientific exchange?
- In what types of forums does scientific exchange typically occur? Should the use of certain forums be given particular significance when determining whether an activity is scientific exchange or an activity that promotes the drug or device? If so, which forums?
- What are the distinctions between scientific exchange and promotion? What are the boundaries between scientific exchange and promotion?
- Generally, who are the speakers involved in scientific exchange, and who is the audience for their communications?

- How do companies generally separate scientific roles and promotional roles within their corporate structures?
- How should the FDA treat scientific exchange concerning off-label uses of already approved drugs and new uses of legally marketed devices? Should there be any distinctions between communications regarding uses under FDA-regulated investigation (to support potential approval) and communications regarding uses that are not under express FDA-regulated investigation?
- How should the FDA treat scientific exchange concerning the use of products that are not yet legally marketed (that is, products that cannot be legally distributed for any use outside of an FDA- or institutional review board-approved clinical trial)?

The FDA will accept comments on the issues raised in this notice until March 27, 2012.

Implications

The standards established in the draft guidance are to a degree unremarkable, and are consistent with the historical standards that have guided manufacturer/distributor responses to unsolicited requests for off-label information—*i.e.*, that it is appropriate for an entity to respond to an unsolicited request for off-label information by providing truthful, balanced, non-misleading and non-promotional scientific or medical information that is responsive to the specific request. Nevertheless, manufacturers and distributors should review their standard operating procedures to evaluate whether their responses to unsolicited requests for information are consistent with the principles laid out in the draft guidance.

It is encouraging that the FDA is engaging with the industry on these issues, which have caused so much controversy and expense in recent years. The agency, in its draft guidance, acknowledges the rapidly evolving world of social media interactions involving patients and physicians, but does not, however, delve deeply into the practical realities of how to manage proactively patient and physician access to information via the internet. The draft guidance is also silent with respect to a number of other important outstanding issues, including how manufacturers should respond to: requests for information (on-label and off-label, solicited and unsolicited) from payers, formulary committees and other similar entities, and requests for third-party clinical practice guidelines (on-label and off-label, solicited and unsolicited) beyond those addressed under the reprints guidance.

The FDA, in the December 28, 2011, *Federal Register* notice, does indicate that it is in the process of considering many of the above-referenced outstanding questions, and appears willing to consider industry comments. As such, manufacturers and/or distributors of FDA-regulated products may wish to consider providing comments regarding the draft guidance and/or in response to the issues raised in the December 28, 2011, *Federal Register* notice.

Clients should contact their regular McDermott Will & Emery lawyer for more information regarding the FDA's draft guidance and request for comments, as well as the implications for their businesses. In particular, clients should consider taking advantage of this opportunity to provide the agency with input on these important issues.