FDA Issues Two Important Documents Concerning Communication of Off-Label Information

Draft Guidance Could Limit Manufacturers' Ability to Respond to Unsolicited Requests During Live Presentations and on the Internet

This week, the Food and Drug Administration ("FDA") issued two important documents relating to drug and device manufacturers' communications about unapproved or uncleared (*i.e.*, off-label) uses of their products. FDA's *Draft Guidance for Industry: Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices ("Draft Guidance")*, issued on December 27, 2011, proposes new recommendations for manufacturers to follow when responding to unsolicited requests for off-label information. A *Federal Register* notice published on December 28, 2011, entitled *Communications and Activities Related to Off-Label Uses of Marketed Products and Use of Products Not Yet Legally Marketed*, responds to a Citizen Petition filed by Ropes & Gray and another law firm on behalf of seven drug and device manufacturers and provides industry with an opportunity to comment on policies regarding scientific exchange.

Draft Guidance on Unsolicited Requests

The *Draft Guidance* addresses the longstanding safe harbor under which FDA does not consider manufacturers' responses to unsolicited requests for information to be evidence of prohibited off-label "intended uses" for drugs or devices. The document reaffirms FDA's position that, for the safe harbor to apply, manufacturers' responses must be truthful, balanced, non-misleading, non-promotional, and tailored to the specific question asked. In addition, the *Draft Guidance* would limit the safe harbor by adopting a narrow definition of what constitutes an "unsolicited" request and by creating a new distinction between "private" and "public" unsolicited requests. It also would, for the first time, establish guidance for responding to unsolicited requests encountered through websites and social media.

Solicited vs. Unsolicited Requests

According to the *Draft Guidance*, unsolicited requests are limited to those initiated by persons or entities "completely independent of the relevant firm" and not "prompted *in any way* by a manufacturer or its representatives." Examples of "solicited" requests include those that:

- Follow a presentation where a manufacturer or its representative (*e.g.*, a paid speaker or medical science liaison) discusses an off-label use;
- Come through a phone number, email address, or website address provided by a manufacturer in a way that implies the availability of off-label information; or
- Are received through a company website with pre-established pull-down menus or general search functions that direct users to off-label information about company products.

The Private/Public Distinction

The *Draft Guidance* would create a new distinction between "private" and "public" unsolicited requests. According to the *Draft Guidance*, when responding to a "private" request (*i.e.*, a "one-on-one" request, such as a question posed by a doctor in a phone call to the company's medical affairs department), a manufacturer should ensure that:

- Medical or scientific staff independent from the sales or marketing department are responsible for generating the response;
- The response is accompanied by a copy of the FDA-required labeling, a complete list of references for all the information disseminated in the response, and prominent statements relating to the approved or cleared use and providing important safety information; and
- Records are kept regarding the requestor's name, contact information, and affiliation, as well as information about the response provided and any follow-up inquiries received.

If a company chooses to respond to a "public" request (*i.e.*, any request that is not one-on-one, such as on an Internet discussion board or at a company-sponsored speaker program), the following recommendations would apply:

- Companies should only respond to unsolicited questions that mention one of its products by name;
- A public response should convey that the question pertains to an unapproved or uncleared use;
- Most notably, *no substantive off-label information should be provided in the response*, even if in response to an unquestionably unsolicited question, regardless of the size or composition of the audience or the medium in which the exchange occurs; rather, the individual asking the question should be invited to follow up with the company's medical or scientific affairs department;
- Company representatives must clearly disclose their involvement with the company; and
- A public response should not be promotional and should include a mechanism for accessing FDA-required labeling (*e.g.*, a link to the FDA-approved package insert).

Effect of the Draft Guidance

The *Draft Guidance*, if finalized, would represent FDA's current thinking on the safe harbor, but communications inconsistent with it would not be *per se* illegal. Such communications could, however, be used as evidence of a new (off-label) intended use. As a result, and because FDA asserts that the *Draft Guidance* merely "clarifies" and is "consistent with" past FDA policy on unsolicited requests, many companies may feel compelled to follow its recommendations, even though not expressly required to do so as a legal matter. Comments and questions about the *Draft Guidance* must be submitted to the Agency by March 26, 2012.

Federal Register Notice on Scientific Exchange

In the *Federal Register* notice, FDA requests that interested parties submit comments regarding the concept of scientific exchange generally and provide responses to a number of specific questions posed by the Agency. The questions cover topics such as the definition of scientific exchange, the distinction between scientific exchange and promotion, and the relevance of speakers and audience, quality of data, and type of drug or device being discussed in determining whether a particular communication is properly considered promotion or scientific exchange.

Comments and questions about the *Federal Register* notice must be submitted to the Agency by March 27, 2012.

If you would like to discuss the foregoing or any other related matter, please contact any member of Ropes & Gray's FDA Regulatory Practice or your usual Ropes & Gray advisor.