

ADVISORY | Food & Drug

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FDA RELEASES DRAFT GUIDANCE ON RESPONDING TO UNSOLICITED REQUESTS FOR OFF-LABEL INFORMATION AND SEEKS STAKEHOLDER INPUT ON SCIENTIFIC EXCHANGE

On December 30, 2011, the Food and Drug Administration (FDA) published a Federal Register notice announcing the availability of a draft guidance entitled “Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices.”¹ The draft guidance describes FDA’s views about how a company should respond to unsolicited requests for off-label information about its approved prescription drugs for human and animal use (including biological products licensed under the Public Health Service Act) and approved or cleared medical devices for humans. Comments on the draft guidance must be submitted by March 29, 2012 to ensure that FDA considers the comment before finalizing the guidance.

In a related development, earlier in the week, on December 28, 2011, FDA opened a docket to accept comments and information related to scientific exchange about off-label uses of approved products and about uses of unapproved products.² Comments must be submitted to the docket by March 27, 2012.

Responding to Unsolicited Requests

Background

Prior to FDA’s draft guidance, FDA’s policy regarding industry responses to unsolicited requests was largely set forth in historic agency statements. For example, in 1982, FDA issued a one-page policy statement taking the position that an unsolicited request for information would be “regarded and treated as a personal communication between the requester and the firm” and the exchanges would not be regulated as labeling.³ In subsequent years, FDA’s policy was restated in several regulatory documents, but prior to the draft guidance, FDA provided few details regarding its unsolicited request policy. The draft guidance, therefore, represents FDA’s most comprehensive description of its unsolicited request policy to date.

In General

The draft guidance addresses only unsolicited requests for off-label information about approved drugs and approved or cleared medical devices. Unsolicited requests about investigational products

¹ 76 Fed. Reg. 82303 (Dec. 30, 2010).

² 76 Fed. Reg. 81508 (Dec. 28, 2010).

³ Position on the Concept of Solicited and Unsolicited Requests (Apr. 22, 1982); see also 59 Fed. Reg. 59820, 59823 (Nov. 18, 1994); 63 Fed. Reg. 64556, 64558 (Nov. 20, 1998).

are not addressed. In the draft guidance, FDA explains that off-label information may be of use not only to healthcare professionals but also to individuals (not only health care providers), who may seek information about a medical product for themselves, patients, family members, or friends. FDA notes that firms often have robust and up-to-date information about their products and recognizes that firms can provide truthful, non-misleading, and accurate responses to questions about their products. As result, the agency explains, a company's response to an unsolicited request for information about its products may be in the best interest of public health.

FDA adds, however, that a response to a request for off-label information that is prompted by a manufacturer or its representative may be considered evidence that the firm intends that the drug or medical device be used for a use that has not been approved or cleared by FDA. FDA's assertion of authority to determine whether dissemination of scientific and medical information constitutes unlawful promotion of a new use therefore has not changed. But FDA recognizes in the guidance that responding to requests for off-label information may, under certain circumstances, advance public health.

Unsolicited Requests

FDA defines an unsolicited request as a request that is not prompted "in any way" by the company or its representative and is initiated by a person or entity that is completely independent of the company. For example, an unprompted email from an individual to medical affairs staff or a post on a product website asking about off-label uses of a company product would be an unsolicited request.

FDA considers a request for off-label information that is prompted by a company or its representative to be solicited. FDA provides eight examples of activities that it considers to be soliciting requests, including: (1) issuing business reply cards specifically offering information about off-label uses of the drug, (2) suggesting a new indication on a commercial exhibit panel, (3) encouraging users of a product to post videos about their experiences using the product, which may result in video postings about an off-label use, and (4) inviting health care professionals to request more information about an off-label use mentioned by a sales representative.

Recommendations

In the draft guidance, FDA identifies two types of unsolicited requests for off-label information—requests made directly and privately to firms (non-public unsolicited requests) and requests made in public forums such as meetings or product websites, discussion boards, chat rooms, or third party websites (public unsolicited requests). FDA recommends different approaches to responding to each type of unsolicited request. The agency's recommendations for non-public requests are consistent with the agency's past statements about unsolicited requests.⁴ This is, however, the agency's first statement on responses to unsolicited requests posted on the Internet and responses to unsolicited requests in other public forums such as a speaker program.⁵

Non-public unsolicited requests. FDA clarifies that a firm that chooses to respond to an unsolicited request for off-label information should provide the final response as a private, one-on-one communication only to the specific individual who requested the information. The agency recommends that information distributed in response to the unsolicited request be truthful, non-misleading, accurate, balanced, non-promotional and scientific in tone and presentation, and

⁴ See, e.g., Position on Unsolicited Requests, *supra* note 3; Current Issues and Procedures, at 7 (Apr. 1994); 59 Fed. Reg. 59820, 59823 (Nov. 18, 1994).

⁵ FDA notes that this is the first of "multiple draft guidances" addressing issues related to social media.

tailored to answer only the specific question asked. The response should provide “non-biased information” about the off-label use, and the firm should disseminate applicable data (e.g., representative publications that reach different conclusions) that do not support, or cast doubt on, the safety or efficacy of the off-label use. Further, the response should include complete copies of the scientific or medical information responsive to the request, rather than a summary prepared by the firm. FDA expresses a preference for the dissemination of peer-reviewed journal articles, medical texts, or data derived from independent sources, but notes that a response can include unpublished data on file at the company. If a journal reprint is disseminated, it should be published by an organization that has a publicly stated (and followed) policy of full disclosure of conflicts of interest or biases for all authors, contributors, and editors.

The response should be distributed separately from information that is promotional in nature, and each response should be accompanied by the product’s approved labeling, as well as a complete list of references. The response should include a prominent statement that the use is not approved or cleared, the FDA-approved indication or cleared intended use statement, and any important safety information. Information about known or suspected risks relevant to the disease or condition for which information was requested should be included. As an example, FDA notes that a request for information about the use of a specific drug during pregnancy in patients with diabetes should include information known to the company about fetal harm caused by that drug when used in pregnant patients with arthritis. Records should be kept of the nature of the request (including the name, address, and affiliation of the requestor), the response provided, and any follow-up questions from the requestor.

FDA also recommends that requests for off-label information be referred to the company’s medical affairs department, which should be staffed with personnel with specialized backgrounds in responding to unsolicited requests for information. The agency recommends that sales representatives, due to their promotional training and experience, provide no input on the content of responses to unsolicited requests for off-label information.

Public requests. FDA suggests that off-label information not be provided publicly in response to an unsolicited request made in a public forum for off-label information about the company’s named product. Rather, FDA recommends that the company state that the question relates to an unapproved or uncleared use of the product and provide contact information (e.g., email address, telephone number, facsimile) for the company’s medical affairs department. The representative responding to the request, who should clearly disclose his or her connection to the company, should provide this information in a non-promotional manner. If the individual privately follows-up with the company (e.g., makes a non-public request), FDA recommends that the company follow the parameters outlined above for responding to a non-public unsolicited request.

Result

FDA states that if a firm follows the recommendations in the draft guidance, the agency does not intend to use the firm’s responses that include off-label information as evidence of intent that the firm’s product be used for the unapproved or uncleared use in question. These responses also would not be expected to comply with the regulatory requirements that apply to promotional labeling and advertising.

Request for Comments About Scientific Exchange

Background

FDA regulations on investigational products provide that the agency does not intend its promotional rules to restrict the “full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media.”⁶ “Scientific exchange” is not defined in the Federal Food, Drug, and Cosmetic Act (FDCA) or in FDA regulations, and over the years FDA has provided only limited guidance on the scope of what it considers “scientific exchange.”

Request for Comments

In July 2011, a group of innovator pharmaceutical companies filed a citizen petition, which is pending, requesting that FDA provide greater clarity on its regulations and policies governing certain communications and activities related to new uses of marketed products and uses of products that are not yet legally marketed. FDA has now established a docket to solicit stakeholder input regarding scientific exchange. The agency is seeking detailed comments “on all aspects of scientific exchange communications and activities related to off-label uses.” FDA has posed specific questions for comment, including how to define scientific exchange, what type of activities constitute scientific exchange, and the boundary between scientific exchange and promotion. Comments must be submitted by March 27, 2012.

If you have any questions concerning the material discussed in this client alert, please contact the following members of our food & drug practice group:

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⁶ 21 C.F.R. § 312.7(a).