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Client Alert

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FDA Issues Guidance on Responding to Unsolicited Requests for Off-label Information about Prescription Drugs and Medical Devices

The Food and Drug Administration (FDA) recently issued a draft guidance entitled "Responding to Unsolicited Requests for Off-label Information about Prescription Drugs and Medical Devices."[1] The guidance, while not legally binding, provides the agency's current thinking on how companies should handle unsolicited requests for off-label information, whether in a public or private forum.[2] Comments to the draft guidance may be submitted to the FDA within 90 days of publication in the *Federal Register*.

The draft guidance confirms the FDA's long-standing policy that pharmaceutical and medical device companies may respond to unsolicited, unprompted requests for off-label information, so long as the response is truthful, objective, non-promotional and narrowly tailored to answer the request, and that such responses do not require compliance with the FDA's promotional and advertising requirements. However, the document also offers some new insight into the agency's treatment of such responses. A few particularly noteworthy points from the guidance include the following:

- Where a request for information is made in a public forum, the company should respond only to the specific requestor, in a private, one-on-one communication. Based on this recommendation, some companies might reconsider the practice of allowing speakers to respond to such questions in public forums, such as at dinner meetings.[3]

- This document is the FDA's first foray into offering guidance on social medial-related issues.[4] Social media tools (such as discussion boards and websites) are one type of public forum where requests for off-label information may arise, and the agency discusses appropriate responses in these and other public venues.

1 The draft guidance is available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM285145.pdf.
2 The draft guidance only applies to dissemination of information about products that are approved or cleared for marketing authorization for some particular use. That is, a request for off-label information refers to any request for information regarding a new use for which approval or clearance would be required. Promotion and commercialization of an investigational product, which not approved for any use remains prohibited.
3 An FDA contact in the Office of Prescription Drug Promotion informally confirmed via phone that the guidance applies to such cases.
4 As noted in a previous AGG Client Alert (found at http://www.agg.com/media/interior/publications/Minsk-Cohen-Good-Things-Come-To-Those-Who-Wait.pdf), the FDA has decided not to issue one guidance document on social media promotional matters, but has instead indicated that it will release several subject-specific guidance documents.

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- The FDA affirms that off-label information requests should be directed to a company's medical affairs department, and sales and marketing should not be involved in the response.

- Responses that conform to the guidance will not be used by the FDA as evidence of the firm's intent that the product be used for an unapproved or uncleared use.

This bulletin summarizes some of the key points from the guidance document.

Determining Whether a Request Is Unsolicited or Solicited

The FDA distinguishes in the guidance between "unsolicited" and "solicited" requests for off-label information. Unsolicited requests are those initiated by persons or entities that are completely independent of the company, while solicited requests are prompted by a manufacturer or a representative (and may be considered evidence of a company's intent that the product can be used in an off-label manner).

The agency also distinguishes between requests made in a non-public (private) versus public forum. The *non-public* unsolicited request is one directed privately to a company using a one-on-one communication approach; a *public* unsolicited request is one made in a public forum, whether directed to the company specifically or to a larger forum. Some examples offered by the FDA include the following:

- ***Non-public unsolicited request***
  An individual calls or emails the company's medical information staff. Neither the request nor the response is visible to the public.

- ***Public unsolicited request***
  - An individual asks a question to the company's representative, such as a speaker, during a live presentation, and the question is heard by other attendees. FDA considers the question and any response before the larger audience to be public.
  - An individual posts on a firm-controlled website or a third-party discussion forum about an off-label use of a specific product.

- ***Solicited request***
  - A sales representative mentions an off-label and invites a healthcare professional to ask for more information.
  - A company representative, such as a medical science liaison or paid speaker, presents off-label use information at a company-sponsored promotional event, such as at a dinner program, and attendees ask for more information.
  - A company asks or encourages users to post videos about their own personal experiences of its product on third-party video-sharing sites, such as YouTube, which, in turn results in requests for information about off-label uses.

— A company announces study results through a microblogging service, such as Twitter, that suggests an off-label use of its product is safe and effective, resulting in requests for information about those uses.

General FDA Policy on Responding to Unsolicited Requests for Off-label Information

The guidance reiterates the FDA's position that companies may respond to unsolicited requests for information, so long as the responses are truthful, balanced, non-misleading, non-promotional and responsive to the specific request. The FDA states in the guidance that such responses should be made only to the specific individual requesting the off-label information as a private, one-on-one communication, regardless of whether the initial unsolicited request for off-label information was made in a non-public or public forum.

This recommendation is particularly noteworthy, because a number of companies allow speakers or consultants to respond to unsolicited requests for off-label information at public forums, such as dinner meetings, where the speaker answers the question, (after qualifying that the use mentioned is not FDA-approved), notes that the response is based on personal, clinical experience, and then returns to the on-label discussion. Companies might want to rethink this practice, in light of the guidance's recommendation that the speaker should direct the questioner to the company's medical affairs group or respond privately to the questioner.

Regarding responses to a *non-public*, unsolicited request for off-label information, the FDA's recommendations include the following:

- Provide the information directly only to the individual making the request.

- Narrowly tailor the response to the question asked, including narrowing the question if it is broad in nature, and provide information about known or suspected risks associated with other diseases or conditions that is relevant to the disease or condition for which information was requested to ensure a complete and accurate presentation of the risk information.

- Provide a truthful, non-misleading, accurate, and balanced response, including articles or texts that reach different or contrary conclusions regarding the use at issue.
  - — Ideally, the company would distribute published, peer-reviewed journal articles, medical texts, or data derived from independent sources, including full disclosure of any conflict of interest or biases for all authors, contributors, or editors associated with the journal or organization.
  - — Information should include *complete* copies of these reprints, texts or other literature, and not merely summary documents or abstracts prepared by the company.
  - — Responses may include unpublished data on file if responsive to the specific request.
  - — Information distributed should be scientific in nature and not promotional.

- Refer questions about off-label uses to the company's medical or scientific representative or department, and ensure that sales and marketing personnel "have no input on the content of responses."

- Include in the response:
  - a copy of the FDA-required labeling, such as the FDA-approved package insert or the FDA-approved patient labeling;
  - a prominent statement notifying the recipient that FDA has not approved or cleared the product as safe and effective for the off-label use;
  - a prominent statement disclosing the indication(s) for which FDA has approved or cleared the product;
  - a prominent statement providing all important safety information; and
  - a complete list of references for all of the information disseminated in the response.

- Maintain records regarding the nature of the request for information (including the name, address, and affiliation of the requester), the information provided, and any follow-up inquiries or questions.

Concerning responses to *public* unsolicited requests for off-label information, the FDA's recommendations include the following:

- Respond only when the request relates specifically to the company's *own* named product (e.g., "Can product X be used for condition Y," which specifically refers to the product name, compared to a non-specific question, such as, "What product can be used for condition Y," where the company should not respond, because the question is not specific to its product.)

- Do *not* include any off-label information when making a public response, such as in a social media forum. Rather, note that the question relates to an off-label use and direct individuals to contact the company's medical/scientific representative or medical affairs department to obtain more information. The FDA notes that the response should not be made to the broader audience, even though the question may have originated in a public forum.

- Provide contact information for the medical or scientific personnel or department, such as an e mail address, telephone number or fax, so that the requester may obtain information through a non-public, one-on-one communication.

- Disclose any involvement that a representative who provides public responses to unsolicited requests for off-label information might have with a particular company and provide the name of the company representative or department to contact for follow-up information in a non-public forum.

- Do not respond in a promotional nature or tone, but can include a means to access current FDA-required labeling. FDA notes that direct link to product websites, product promotional materials, firm websites, third-party websites, or a URL or web address that, by name alone, may be promotional in nature (e.g., www.bestcancercure.com) should not be provided.

Conclusion

The draft guidance is essentially a written articulation of existing policies and long-standing industry best practices regarding responses to unsolicited requests for off-label information. However, the document offers a few new insights for consideration. For example, the guidance specifies which departments in the company should handle these requests, how the responses should be tailored, and what type of information should be included. Responses that follow these guidelines will not be interpreted by the FDA as attempts to promote unapproved or uncleared product use.