4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2011-D-0868]

Draft Guidance for Industry on Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled "Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices." This draft guidance responds to stakeholder requests for specific guidance on FDA's current views on how manufacturers and distributors (firms) of prescription human and animal drug products and medical devices can respond to unsolicited requests for information about unapproved or uncleared indications or conditions of use (off-label information) related to their FDA-approved or cleared products. This draft guidance updates and clarifies FDA's policies on unsolicited requests for off-label information, including those that firms may encounter through emerging electronic media.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comments on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]. Submit written comments on the proposed collection of information

by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Submit written requests for single copies of the draft guidance to the Office of Communications, Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993-0002; to the Office of Communication, Outreach and Development (HFM-40), Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852-1448; to the Communications Staff, Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Pl. (HFV-12), Rockville, MD 20855; or to the Division of Small Manufacturers, International and Consumer Assistance, Office of Communication, Education and Radiation Programs, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, rm. 4613, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "Responding to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices." In July 2011, FDA received a citizen petition, filed on behalf of seven prescription drug manufacturers, seeking additional clarification on several areas of FDA policy regarding distribution of information about prescription drugs. One of the areas was how to respond to unsolicited requests from health care professionals or consumers for information about off-label uses of approved products.

In addition, on November 12 and13, 2009, FDA held a Part 15 public hearing on "Promotion of FDA-Regulated Medical Products Using the Internet and Social Media Tools" to provide an opportunity for broad public participation and comment on the following questions that relate specifically to promotional issues: (1) For what online communications are manufacturers, packers, or distributors accountable? (2) How can manufacturers, packers, or distributors fulfill regulatory requirements (e.g., fair balance, disclosure of indication and risk information, post-marketing submission requirements) in their internet and social media promotion, particularly when using tools that are associated with space limitations and tools that allow for real-time communications (e.g., microblogs, mobile technology)? (3) What parameters should apply to the posting of corrective information on Web sites controlled by third parties? (4) When is the use of links appropriate? Subsequent to the live testimony heard at the

Part 15 public hearing, FDA received 72 comments to the docket. This draft guidance is the first of multiple draft guidances the Agency plans to publish that address questions and issues related to emerging electronic media.

This draft guidance provides FDA's recommendations to firms wishing to respond to unsolicited requests for off-label information about their products, including both requests made directly and privately to firms and requests made in public forums, including through emerging electronic media. This draft guidance discusses the difference between unsolicited and solicited requests and presents a number of examples of both types of requests. If a firm responds to unsolicited requests for off-label information in the manner described in this draft guidance, FDA does not intend to use such responses as evidence of the firm's intent that its product be used for an unapproved or uncleared use. Such responses also would not be expected to comply with the disclosure requirements related to promotional labeling and advertising. Firms may choose to respond to unsolicited requests for information about off-label uses of their approved or cleared products in a manner other than that recommended in this draft guidance. Such activity would not constitute a per se violation of the law, but could potentially be introduced as evidence of a new intended use.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the Agency's current thinking on responding to unsolicited requests for off-label information about prescription drugs and medical devices. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. The Paperwork Reduction Act of 1995

Under the Paperwork Reduction Act of 1995 (the PRA) (44 U.S.C. 3501-3520), Federal agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information they conduct or sponsor. "Collection of information" is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes Agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal agencies to provide a 60-day notice in the Federal Register concerning each proposed collection of information before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information set forth in this document.

With respect to the following collection of information, FDA invites comments on these topics: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information collected; and (4) ways to minimize the burden of information collected on the respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Title: Industry Responses to Unsolicited Requests for Off-Label Information About Prescription Drugs and Medical Devices.

Description of Respondents: Respondents to this collection of information are manufacturers and distributors (firms) of prescription human and animal drug products or medical devices.

Burden Estimate: The draft guidance pertains to the dissemination of scientific or medical information about off-label uses for approved or cleared products by FDA-regulated industry when it responds to (1) non-public unsolicited requests for off-label information made directly and privately to them, or (2) public unsolicited requests for off-label information, including those that firms may encounter through emerging electronic media.

The draft guidance explains that FDA's current policy position is that, regardless of whether the initial unsolicited request for off-label information was made in a non-public or public forum, FDA does not intend to use the firm's actions as evidence of a new intended use, nor expect distributed materials to conform to existing regulatory requirements for promotional labeling or advertising, if the firm responds in the manner outlined in the guidance. Specifically, the draft guidance recommends that a firm that chooses to respond to an unsolicited request for off-label information provide the final response containing the requested off-label information about its product only to the specific individual who requested the information as a private, one-on-one communication. FDA also recommends that information distributed in response to an unsolicited request be truthful, non-misleading, accurate, balanced, and non-promotional scientific or medical information that is tailored to answer only the specific question asked, even if responding to the request requires the firm to provide information regarding unapproved or uncleared indications or conditions of use. To meet this standard, the draft guidance recommends that firms disclose certain information to others when responding to their unsolicited requests. This "third-party disclosure" constitutes a "collection of information" under the PRA. In addition, the PRA is triggered because the draft guidance also recommends that firms maintain certain records related to this disclosure.

Non-public responses

When providing non-public responses to unsolicited requests for information about unapproved or uncleared indications or conditions of use, the draft guidance recommends the following:

- A response should provide non-biased information or data relating to the particular off-label use that is the subject of the request, including applicable data that are not supportive or that cast doubt on the safety or efficacy of that use. For example, when conclusions of articles or texts that are disseminated have been specifically called into question by other articles or texts, a firm should disseminate representative publications that reach contrary or different conclusions regarding the use at issue. The response should include complete copies of scientific reprints, technical literature, or other scientific and medical information responsive to the request, not just summary documents or abstracts prepared by the firm. The response may include unpublished data on file if they are responsive to the specific request (either supporting or casting doubt on the safety or efficacy of the off-label use). However, to the greatest extent possible, a firm should rely on published peer-reviewed journal articles, medical texts, or data derived from independent sources. To the extent the response consists of published reprints from journals, those reprints should be from journals that have a publicly stated policy, to which the organization adheres, of full disclosure of any conflict of interest or biases for all authors, contributors, or editors associated with the journal or organization.

In addition to responsive materials as described previously in this document, the guidance recommends that the following information be provided to the requestor:

1. A copy of the FDA-required labeling, if any, for the product (e.g., FDA-approved package insert and, if the response is for a consumer, FDA-approved patient labeling or, for new animal drugs, FDA-approved client information sheet).

2. A prominent statement notifying the recipient that FDA has not approved or cleared the product as safe and effective for the use addressed in the materials provided.

3. A prominent statement disclosing the indication(s) for which FDA has approved or cleared the product.

4. A prominent statement providing all relevant safety information including, if applicable, any boxed warning for the product.

5. A complete list of references for all of the information disseminated in the response (e.g., a bibliography of publications in peer-reviewed medical journals or in medical or scientific texts; citations for data on file, for summary documents, or for abstracts).

Finally, the draft guidance recommends that a firm maintain the following related records:

1. The nature of the request for information, including the name, address, and affiliation of the requestor.

2. Records regarding the information provided to the requestor.

3. Any followup inquiries or questions from the requestor.

Public responses

When providing public responses to unsolicited requests for information about unapproved or uncleared indications or conditions of use, the draft guidance recommends that the following information be disclosed to the requestor:

1. A firm's public response to public unsolicited requests for off-label information about its named product should convey that the question pertains to an unapproved or uncleared use of the product and be limited to providing the firm's contact information for the medical or scientific personnel or department so that individuals can follow up independently with the firm to obtain specific information about the off-label use of the product through a non-public, one-on-one communication. After an individual has privately contacted the firm for more information regarding an off-label use of the firm's product, the firm should provide a detailed response and maintain records following the parameters outlined in Section V of the draft guidance (and summarized previously in this document for non-public responses to unsolicited requests).

2. Representatives who provide public responses to unsolicited requests for off-label information should clearly disclose their involvement with a particular firm.

3. Public responses to public unsolicited requests for off-label information should not be promotional in nature or tone and should include a mechanism for providing readily accessible FDA-required labeling, if any, for the product (e.g., FDA-approved package insert and, if the response is for a consumer, FDA-approved patient labeling or, for new animal drugs, FDA-approved client information sheet).

FDA estimates that approximately 400 firms respond annually to approximately 40,000 non-public unsolicited requests for off-label information made directly and privately to them as well as to public unsolicited requests for off-label information, including those that firms may encounter on emerging electronic media. FDA estimates that it will take firms approximately 4 hours to provide responses to each unsolicited request for off-label information as recommended in the draft guidance.

FDA also estimates that approximately 40,000 records will be maintained for all responses to non-public and public unsolicited requests for off-label information, and that each record will take approximately 15 minutes to prepare and maintain.

Table 1.--Estimated Annual Reporting Burden[1]

Draft Guidance on Responding to Unsolicited Requests for Off-Label Information	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Responses to non-public and public unsolicited requests	400	100	40,000	4	160,000

1 There are no capital costs or operating and maintenance costs associated with this collection of information.

Table 2.--Estimated Annual Recordkeeping Burden[1]

Draft Guidance on Responding to Unsolicited Requests for Off-Label Information	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
Records related to responses to non-public and public unsolicited requests	400	100	40,000	.25	10,000

1 There are no capital costs or operating and maintenance costs associated with this collection of information.

III. Comments

Interested persons can submit to the Division of Dockets Management (see ADDRESSES) either electronic or written comments regarding this document. It is only necessary to send one set of comments. It is no longer necessary to send two copies of mailed comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

IV. Electronic Access

Persons with access to the Internet may obtain the document at either http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm, http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm, http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/default.htm,

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm, or http://www.regulations.gov.

Dated: December 27, 2011.

Leslie Kux,

Acting Assistant Commissioner for Policy.

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