4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2014-D-0758]

Draft Guidance for Industry on Distributing Scientific and Medical Publications on Risk Information for Approved Prescription Drugs and Biological Products--Recommended Practices; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled "Distributing Scientific and Medical Publications on Risk Information for Approved Prescription Drugs and Biological Products--Recommended Practices." This guidance describes FDA's current thinking on recommended practices for drug manufacturers and their representatives to follow when distributing to health care professionals or health care entities scientific or medical journal articles that discuss new risk information for approved prescription drugs for human use, including drugs licensed as biological products, and approved animal drugs. The recommendations in this draft guidance are intended to address issues specific to the distribution of new information about risks associated with a drug that further characterizes risks identified in the approved labeling.

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comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 75 DAYS AFTER DATE OF PUBLICATION IN THE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ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201,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; Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 3128, Silver Spring, MD 20993-0002; or to Communications Staff (HFV-12), Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Pl., Rockville, MD 20855. 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:

Regarding prescription drugs: Lauren Wedlake, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 6328, Silver Spring, MD 20993-0002, 301-796-2500.

Regarding prescription biological products: Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911.

Regarding animal drugs: Dorothy McAdams, Center for Veterinary Medicine (HFV-216), 7519 Standish Pl., Rockville, MD 20855, 240-453-6802.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "Distributing Scientific and Medical Publications on Risk Information for Approved Prescription Drugs and Biological Products--Recommended Practices." In February 2014, FDA issued a draft guidance entitled "Distributing Scientific and Medical Publications on Unapproved New Uses--Recommended Practices" to clarify the Agency's position on manufacturer dissemination of scientific or medical publications--including scientific or medical journal articles, scientific or medical reference texts, and clinical practice guidelines--that include information on unapproved new uses of the manufacturer's products. Stakeholders have raised questions regarding the Agency's position on manufacturer dissemination of new scientific or medical information about safety information contained in the labeling for approved drugs. Because this concerns dissemination of new risk information related to approved uses of a drug, this issue is distinct from the dissemination of information on unapproved new uses of approved drugs. In response to those questions, the Agency is issuing this draft guidance to clarify and solicit public comments on the Agency's position on manufacturer dissemination of new risk information regarding lawfully marketed drugs for approved uses to health care professionals or health care entities.

FDA recognizes that the safety profile of a drug evolves throughout its lifecycle as the extent of exposure to the product increases and that it can be helpful for health care practitioners to receive significant new risk information about an approved product in a timely manner. FDA

anticipates that the earliest distribution of new risk information will generally involve distribution of recently published studies, as opposed to textbooks or clinical practice guidelines. Accordingly, FDA is providing guidance for manufacturers that choose to distribute new risk information in the form of a reprint or digital copy of a published study.

FDA believes that recommendations specific to the distribution of risk information are needed for two reasons:

- In general, there are differences in the purpose, nature, and reliability of the evidence used to determine the effectiveness of a drug (e.g., to support a new intended use) and the evidence that is the basis for a product's risk assessment. Therefore, FDA believes guidance is needed to address the spectrum of data sources that could be appropriate for distribution to provide new risk information.
- New risk information may contradict or otherwise deviate from the risk information in the approved labeling, which may cause confusion or otherwise contribute to patient harm. If the new information is unreliable or presented without the appropriate context, it could influence prescribing decisions or patient monitoring in a manner that could harm patients. Therefore, FDA is proposing recommendations for study or analysis and distribution criteria to help ensure that new risk information that rebuts, mitigates, or refines risk information in approved labeling meets appropriate standards for reliability and is presented with appropriate disclosure of its limitations.

The guidance is being issued in draft to enable public comment on the proposed recommendations.

In light of emerging case law, in particular the case law involving the First and Fifth Amendments of the United States Constitution, FDA is currently engaged in a comprehensive

review of its regulations and guidance documents in an effort to harmonize the fundamental public health interests underlying FDA's mission and statutory framework with interests in the dissemination of truthful and non-misleading information. This draft guidance on distribution of risk information about approved prescription drugs and biological products is a part of that effort. This draft guidance does not address medical devices. FDA also plans to issue, by the end of the calendar year, additional guidance that addresses manufacturer responses to unsolicited requests, distributing scientific and medical information on unapproved new uses, manufacturer discussions regarding scientific information more generally, and distribution of health care economic information to formulary committees and similar entities.

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 "Distributing Scientific and Medical Publications on Risk Information for Approved Prescription Drugs and Biological Products--Recommended Practices." 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

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 that 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 for each proposed collection of information before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing this notice of the proposed collection of information set forth in this document. This draft guidance also refers to previously approved collections of information found in FDA regulations.

With respect to the following collection of information, FDA invites comments on these topics: (1) Whether the proposed information collected 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: Recommendations for Distributing Scientific and Medical Publications on Risk Information for Approved Prescription Drugs and Biological Products.

Description of Respondents: Respondents to this collection of information are manufacturers of approved prescription drugs for human use, including drugs licensed as biological products, and approved animal drugs, and their representatives (firms).

Burden Estimate: The draft guidance pertains to the distribution, by firms, of scientific and medical publications that discuss new risk information for approved prescription drugs for human use and approved animal drugs (including prescription, non-prescription, and Veterinary Feed Directive drugs) marketed in the United States. The draft guidance recommends that if firms choose to distribute scientific and medical publications reflecting new risk information,

those publications should have certain characteristics and certain other information should be distributed with them. Accordingly, the guidance recommends a "third-party disclosure" that constitutes a "collection of information" under the PRA.

If firms choose to distribute new risk information that rebuts, mitigates, or refines risk information in the approved labeling, and the information is in the form of a reprint or digital copy of a published study, the guidance provides recommendations regarding the characteristics of those publications. Specifically, with respect to the data source:

- The study or analysis should meet accepted design and other methodologic standards for the type of study or analysis (e.g., provides a clear description of the hypothesis tested, acknowledges and accounts for potential bias and multiplicity) and should be sufficiently well-designed and informative to merit consideration in assessing the implications of a risk.
- To rebut a prior determination (reflected in the approved labeling) that there is some basis to believe there is causal relationship between the drug and the occurrence of an adverse event, or to otherwise mitigate a described risk, the study or analysis should also be at least as persuasive as the data sources that underlie the existing risk assessment of causality, severity, and/or incidence of the adverse reaction as reflected in approved labeling (e.g., data from a new controlled trial designed to estimate the relative risk of the event, a pharmacoepidemiologic study that is capable of reliably estimating the relative risk, or a rigorous meta-analysis of all relevant data from new and existing controlled trials).
- The conclusions of the study or analysis should give appropriate weight and consideration to, and should be a fair characterization of, all relevant information in the

safety database, including contrary or otherwise inconsistent findings. There is a broad spectrum of potential data sources that can contribute in some way to characterization of a product's safety; new risk information should be considered in light of all relevant existing information and integrated with that data to the extent possible.

- The study or analysis should be published in an independent, peer-reviewed journal.

The draft guidance also makes recommendations with respect to the distribution of the reprint or digital copy, including the recommendation that a cover sheet accompany the reprint or digital copy that clearly and prominently discloses the following:

- The study design, critical findings, and significant methodologic or other limitations of the study or analysis that may limit the persuasiveness or scope of findings that rebut, mitigate, or refine risk information in the approved labeling. Limitations should be discussed in relation to the specific circumstances of the study and its conclusions about a risk.
- The information is not consistent with certain risk information in the approved labeling (should specifically identify the inconsistent information).
- FDA has not reviewed the data.
- Any financial interests or affiliations between the study author(s) and the firm.

The reprint or digital copy should be accompanied by the approved labeling for the product, and when distributed, should be separate from any promotional material. Any statements made by a representative of the firm to a recipient concerning the reprint should be consistent with its content and the information in the disclosure cover sheet.

Additionally, FDA notes in the draft guidance that the recommendations in the guidance do not change a firm's existing obligations to revise its approved labeling in accordance with 21

CFR 201.56(a)(2), 314.70, 514.8(c) and 601.12. As described in this section of the document, this recommendation refers to previously approved collections of information found in FDA regulations. FDA estimates that approximately 500 firms annually distribute scientific and medical publications that discuss new risk information for approved prescription drugs. FDA also estimates that each firm would include some or all of the additional information described previously when distributing annually a total of approximately 4,250 scientific or medical journal articles that discuss new risk information for approved prescription drugs. FDA estimates that it will take each firm approximately 16 hours to make the disclosures recommended in this draft guidance, which includes the time needed to determine whether the article complies with the guidance recommendation on the characteristics of the scientific and medical publications that companies distribute, to determine financial conflicts of interest, to prepare the disclosure statements, and to attach the product labeling.

Table 1.--Estimated Annual Third-Party Disclosure Burden[1]

Draft Guidance on Distributing Scientific and Medical Publications on Risk Information for Approved Prescription Drugs and Biological Products--Recommended Practices	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
Distribution of scientific and medical publications on risk information	500	8.5	4,250	16	68,000

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

This draft guidance also refers to previously approved collections of information found in FDA regulations with respect to submitting supplements to approved applications. These collections of information are subject to review by OMB under the Paperwork Reduction Act of

1995 (44 U.S.C. 3501-3502). The collection of information in 21 CFR 201.56(a)(2) has been approved under OMB control number 0910-0572; in 21 CFR 314.70 has been approved under OMB control number 0910-0001; in 21 CFR 601.12 has been approved under OMB control number 0910-0338; and in 21 CFR 514.8(c) has been approved under OMB control number 0910-0032.

III. Comments

Interested persons may submit either electronic comments regarding this document to http://www.regulations.gov or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of 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, and will be posted to the docket at http://www.regulations.gov.

IV. Electronic Access

Persons with access to the Internet may obtain the document at 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, or http://www.regulations.gov.

Dated: June 6, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

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