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Client Alert

FDA & Life Sciences Practice Group

January 28, 2014

FDA Issues Final Guidance Regarding Dear Health Care Provider (DHCP) Letters

Recommendations are Intended to Improve the Communication of Important New or Updated Safety Information for Prescription Drugs and Biological Products

On January 23, 2014, the Food and Drug Administration (FDA) announced in the Federal Register[1] that it issued a final Guidance for Industry and FDA Staff entitled, "Dear Health Care Provider Letters: Improving Communication of Important Safety Information."[2] The guidance provides specific recommendations on the content and format of DHCP letters that are sent by manufacturers or distributors to physicians and other Health Care Providers (HCPs) to communicate important new or updated safety information about (1) an important drug warning, (2) a change in prescribing information, or (3) a correction of misinformation in promotional labeling or advertising for a prescription drug or biologic product. The guidance also provides instructions regarding what should not be included in DHCP communications. In addition, the agency advises that manufacturers or distributors should conduct, for the company's use, an assessment of the letter's impact on communicating new information to HCPs.

Like all FDA guidance documents, this guidance does not establish legally enforceable responsibilities and failure to adhere to it does not create a *per se* violation of the Federal Food, Drug, and Cosmetic Act. Rather, the guidance provides FDA's specific recommendations to industry on the content and formatting of DHCP letters sent by manufacturers or distributors that can help ensure adherence with the underlying legal requirements.

Background

The guidance finalizes the draft guidance issued on November 12, 2010. The guidance was developed to address the agency's concern that DHCP letters have not consistently met the specifications that are set forth in 21 C.F.R. 200.5 regarding the mailing of important information regarding a drug warning, changes in prescribing information, and correction of advertising and labeling. Whereas FDA must comply with these specifications when distributing such mailings to physicians and others responsible for patient care, manufacturers and distributors are asked to adhere to these specifications. The guidance also addresses the agency's

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concerns that, in some instances, HCPs have not been notified or have not understood new information due to the DHCP letter's content and length and that letters have been "sent for the wrong reasons." In addition to the FDA's experience in risk communication, the guidance was informed by a formal study that examined factors that correlated with physician understanding of new information in a group of DHCP letters distributed during 2000 and 2001.[3] The agency observes that the concepts in the guidance may also be applicable in the development of materials to meet communication plan requirements for Risk Evaluation and Mitigation Strategies (REMS) pursuant to section 505-1(e)(3) of the Federal Food, Drug, and Cosmetic Act.

Acknowledging contemporary modes of correspondence, FDA clarifies that DHCP letters may be distributed by electronic means as well as postal mailing, and are often also made available on the internet though company, professional society, or patient advocacy group websites.

Consultation with FDA

The guidance recommends that manufacturers consult with the appropriate review division (e.g., the Offices of Drug Evaluation or the Office of Generic Drugs) during the development of a DHCP letter to determine (1) whether a DHCP letter should be used, (2) the target HCP audience, (3) how to present the new information "to ensure that the letter clearly and accurately reflects both the manufacturer's and FDA's understanding of the issue and the action required", and (4) the time frame for distribution of the letter. FDA advises that a purpose of consultation is to "help ensure FDA's concurrence that the content of the letter is not in some way false or misleading."

When to Issue a DHCP Letter

DHCP letters should be used to communicate new information in three specific types of letters that are described in 21 C.F.R. 200.5. Model letters are provided for each of the following types of DHCP letters that are specified in the regulation:

- ***Important Drug Warning Letters.*** FDA clarifies that Important Drug Warning Letters should be used to convey major new safety information that "concerns a risk to health", including new information that is being incorporated into the following sections of the labeling: BOXED WARNING, WARNINGS, CONTRAINDICATIONS, or WARNINGS AND PRECAUTIONS. An Important Drug Warning Letter should also be used to communicate the implementation of a new or modified REMS.

- ***Important Prescribing Information Letters.*** These letters should be used to communicate important changes in prescribing information that comprise a change in the INDICATIONS AND USAGE statement that pertains to minimization of risk, improving effectiveness, or a limitation of the indications. It should also be used to communicate a modification in the dose or dosing regimen intended to minimize risk or improve effectiveness. In addition, this type of DHCP letter should be used to communicate a drug shortage issue.

  In contrast, FDA warns that an Important Prescribing Information Letter should not be used to "merely announce a new indication, even an important one."

- ***Important Correction of Drug Information Letters.*** These letters link to FDA enforcement actions and should be used to correct false or misleading information in prescription drug promotional labeling and advertising that is the subject of a Warning Letter or other agency enforcement action.

Recommended Content and Format of a DHCP Letter

FDA recommends that the DHCP letter should identify the target HCP audience and clearly communicate the following four elements at the beginning of the communication: (1) purpose (e.g., informing prescribers about a specific new drug safety issue, (2) description of the new information, (3) existing information that has changed or is

no longer valid, and (4) actions for a HCP to take in response to the new information, if any. The guidance emphasizes that it is usually not sufficient to simply state that labeling has changed and append the new labeling. Contact information should be provided. In addition, if the letter addresses an adverse reaction, it should contain specific contact information for the reporting of new cases to both the manufacturer and FDA.

In general, FDA advises that the letter should not exceed two pages or comparable length of electronic content or the electronic format equivalent.

- ***Instructions regarding seven components of content and their formatting.*** For each of the three types of DHCP letters specified in 21 C.F.R. 200.5, the guidance provides separate detailed instructions regarding the following components of content and how they are to be formatted:

    - *Envelope and Letter Heading,* which is the statement that should appear on the envelope and its format pursuant to 21 C.F.R. 200.5, and which FDA recommends be repeated in similar format as the "header" of the letter or the electronic communication;

    - *Addressees (the target audience*), which should include the full range of HCPs who are likely to dispense or administer the drug, may be providing care for the patient (e.g., emergency department staff in the event of care for an adverse event), or may be distributing the drug under the introduction of a new medication guide pursuant to a REMS (e.g., pharmacists);

    - *Subject Line,* which should include the drug's proprietary and established names, concise description of the safety issue, characterization of its seriousness, the population at risk, and descriptor of increase in the magnitude or rate of the risk, if known;

    - *Initial First and Second Paragraphs,* which are intended to summarize the information that is essential to the HCP's understanding of (1) the description of the issue and (2) actions required to address the issue, if any, including actions to be taken by HCPs and counseling to be provided to patients;

    - *Interior Paragraphs,* which are intended to provide additional information that would help HCPs understand the issue, such as a summary of the data that is the basis for the new safety warning and limitations of the data (what is and is not yet known);

    - *For Correction of Drug Information Letters,* nine specific elements are recommended, and among these are the statement that the information was the subject of a Warning Letter or other action by FDA, where and how the incorrect information was communicated to HCPs, that the information was "deemed false and misleading and why it was false or misleading", and corrected information;

    - *Final Paragraph,* which should include, to the extent relevant, (1) how to report new cases of the adverse reaction or other safety issue discussed in the letter, (2) company contact information for direct queries regarding the safety issue, and (3) FDA contact information.

- ***Reference to full prescribing information.*** In all DHCP letters, FDA states that reference to the full prescribing information should be enclosed in the letter, as well as the medication guide or other approved patient information, if any.

- ***Information that should not be in any DHCP letter.*** The agency cautions that the letter should not include any promotional information. It also advises that the letter should not include information that could obscure or divert attention from the critical safety information, including but not limited to market information, details

about a clinical study design, information about a safety review panel, and plans to investigate the problem if not specifically related to safety.

Assessment of Impact of the DHCP Letter

Although manufacturers are familiar with the use of DHCP letters to communicate important new safety information about prescription drugs and biological products, a novel component of the guidance is the recommendation that manufacturers should conduct an evaluation, **for their own use**, of the impact of the DHCP letter. FDA advises that the impact assessment should evaluate the extent to which the target audience received the letter and is aware of the information communicated in the letter. These concepts parallel those in FDA recall guidance in 21 C.F.R. 7.42 (b)(3) regarding the conduct of *effectiveness checks* in a voluntary recall to verify that the target consignees received notification and understood the information to take appropriate actions.

If the DHCP letter is a component of a REMS, there must be an evaluation plan in place, as specified in the REMS, that is carried out by the manufacturer.

Considerations for Manufacturers

Manufacturers of prescription drugs and biological products should consider conducting a review of current policies and procedures regarding the development and distribution of DHCP letters, including an analysis of previous DHCP letters distributed by the company, to determine if modifications of procedures and training may be appropriate to more closely align with current FDA expectations. It is particularly noteworthy that FDA advises consultation with the agency to determine if distribution of a DHCP letter is appropriate and if so, to ensure that the proposed content is not false and misleading. Manufacturers should also take careful note of FDA's expectation that DHCP letters not be written in a manner that the agency would consider "promotional" or risk obscuring.

Although not mandated by regulations, except in the case of a REMS, some manufacturers may be considering and developing for the first time processes for *impact assessments* to evaluate the effectiveness of the DHCP letter in reaching the target HCP audience and communicating the new information. Although the guidance indicates that the impact assessment is for the manufacturer's "own use", the guidance does not clarify whether this assessment may be treated as an internal audit or if the assessment's findings are intended to be subject to later FDA inspection and review.

The guidance may also be of interest to manufacturers of prescription medical devices. Although the focus of the guidance is prescription drugs and biological products, the precepts regarding organization and formatting to enable concise and effective communications to HCPs may also be applicable to DHCP letters regarding new or updated safety information for prescription medical devices.

Comments regarding this final guidance document may be submitted electronically or in writing to the Division of Dockets Management.[4] King & Spalding would be pleased to assist in preparing such comments which will be publicly posted to the docket.

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[1] 79 Fed. Reg. 3827 (January 23, 2014).

[2] The guidance is accessible at **http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM233769.pdf?source=govdelivery&utm_medium=email&utm_source=govdelivery**

[3] Mazor KM et al. "Communicating Safety Information to Physicians: An Examination of Dear Doctor Letters." *Pharmacoepidem. Drug Safe*. 2005; 14:869-875.

[4] Electronic comments may be submitted to **http://www.regulations.gov** with reference to Docket No. FDA-2010-D-0319.