Guidance for Industry

Questions and Answers Regarding the Labeling of Nonprescription Human Drug Products Marketed Without an Approved Application as Required by the Dietary Supplement and Nonprescription Drug Consumer Protection Act

DRAFT GUIDANCE

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For questions regarding this draft document contact Walter Ellenberg at 301-796-2090.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

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I. INTRODUCTION

This document is intended to assist industry in complying with the labeling requirements of the Dietary Supplement and Nonprescription Drug Consumer Protection Act (Public Law 109-462, 120 Stat. 3469). The statute created a new section 502(x) in the Federal Food, Drug, and Cosmetic Act (the Act). These requirements apply to manufacturers, packers, and distributors of nonprescription (over-the-counter (OTC)) human drug products marketed without an approved application. In particular, this document covers the following topics: (1) the meaning of "domestic address" for purposes of the labeling requirements of section 502(x) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 352(x)); (2) FDA's recommendation for the use of an introductory statement before the domestic address or phone number that is required to appear on the product label under section 502(x) of the Act; and (3) FDA's intent regarding enforcing the labeling requirements of section 502(x) of the Act.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

[1] This guidance has been prepared in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration.

II. BACKGROUND

Public Law 109-462, the Dietary Supplement and Nonprescription Drug Consumer Protection Act, was signed by the President on December 22, 2006.[2] Public Law 109-462 amends the Act to add reporting, recordkeeping, and labeling requirements for OTC drug products that are marketed without an approved application under section 505 of the Act (21 U.S.C. 355).[3] This draft guidance document contains questions and answers relating to these new labeling requirements.

III. QUESTIONS AND ANSWERS

Q1: What information must be included on the label of an OTC drug marketed without an approved application for purposes of complying with section 502(x) of the Act?

Section (d) of Public Law 109-462 adds section 502(x) to the Act to require the label of an OTC drug marketed in the United States without an approved application to include "a domestic address or domestic phone number through which the responsible person [i.e., the manufacturer, packer, distributor, or retailer identified on the drug label] … may receive a report of a serious adverse event" associated with the use of the drug product. If the label does not include the required domestic address or phone number, the drug is misbranded.

When the responsible person chooses to provide a domestic address (rather than a phone number) for adverse event reporting, FDA concludes that the statute requires the product label to bear a full U.S. mailing address that includes the street address or P.O. Box, and the city, state, and zip code of the responsible person. FDA finds that Congress's use of the term "domestic address" in section 502(x) of the Act is a clear and unambiguous directive that labels of OTC drug products marketed without an approved application include all information necessary to enable a serious adverse event report to reach the responsible person. This reading of section 502(x) of the Act is supported by dictionary definitions of "address," which include "the indication of destination, as on mail or parcels" and "the location at which a person or an organization may be reached."[4] Indeed, an address does not serve its intended purpose unless it includes all the information necessary to enable mail to reach its destination.

Similarly, when the responsible person chooses to provide a domestic phone number for adverse event reporting, FDA concludes that the statute requires the phone number on the product label to include the area code. Without the area code, the phone number is incomplete and does not serve its intended purpose of enabling the consumer to contact the responsible person to report a serious adverse event.

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[2] See : *http://www.fda.gov/cder/regulatory/default.htm#Legislation* (*http://www.fda.gov/cder/regulatory/public_law_109462.pdf*)..

[3] Section 760 of the Act (21 U.S.C. 379aa), as amended, provides for mandatory safety reporting for OTC human drug products not subject to applications approved under section 505 of the Act (new drug applications (NDAs) or abbreviated new drug applications (ANDAs)). Accordingly, these new requirements apply to all OTC drug products marketed under the OTC Drug Review, including those not yet subject to a final monograph.

[4] *Webster's II New Riverside University Dictionary* (Houghton Mifflin 1984), p. 77.

Congress's use of the phrase "through which the responsible person … may receive a report" to modify "domestic address or domestic phone number" further supports FDA's conclusion that a complete address or phone number must be provided. This phrase shows Congress's intent that the domestic address or phone number on the label be sufficient to ensure that the responsible person will actually receive the serious adverse event reports that consumers submit. If the address provided on the product label for adverse event reporting is incomplete (e.g., no street address or P.O. Box), it is likely that some of the serious adverse event reports that are submitted to the responsible person by mail will not be received. In addition, when consumers notice the incomplete address, they may decide not to submit a report to the responsible person because they believe it will not be received. Similarly, phone numbers typically require an area code to effectively connect to the responsible person.

The use of the term "domestic address" in section 502(x) of the Act contrasts with Congress's use of a different term, "place of business," in section 502(b) of the Act. Section 502(b) of the Act provides that a drug is misbranded unless the product label bears the name and place of business of the manufacturer, packer, or distributor. FDA regulations interpret "place of business" to require only city, state, and zip code to appear on the product label, as long as the street address is listed in a current telephone directory or other city directory (21 CFR 201.1(i)). The use of the term "domestic address" in section 502(x) of the Act demonstrates Congress's intent to require the responsible person's full address, including the street address or P.O. Box, to appear on the label when the responsible person has opted to receive serious adverse event reports by mail. If Congress had considered the less complete address already required under the "place of business" labeling regulation to be adequate for serious adverse event reporting, there would have been no need to impose a new, more specific requirement in section 502(x) of the Act for the responsible person's "domestic address" to appear on labels.

Q2: Should the label of an OTC drug marketed without an approved application include language indicating that the purpose of the domestic address or phone number is to report serious adverse events associated with the use of the product?

Although section 502(x) does not require the label to include anything other than a domestic address or phone number for the responsible person, FDA recommends that the label bear a clear, prominent statement informing consumers that the domestic address or phone number is for reporting serious adverse events associated with use of the product.

When the responsible person chooses to provide a domestic address (rather than phone number), regardless of whether the address is introduced with a prefatory statement, the full address should be included either (1) under the "Other Information" heading described under section 201.66(c)(7), or (2) outside of "Drug Facts," such as the location on the label that identifies the manufacturer's "place of business."[5] Under these circumstances, the label may include an introductory statement, such as "Reports of serious side effects associated with use of the product can be sent to: [street or P.O. Box, city, state and zip code]."

[5] In this case, the full address satisfies the labeling requirements in section 502(x) and section 505(b)(1) of the Act, as defined further in section 21 CFR 201.1(i).

Currently, under FDA's "Drug Facts" regulations, the labels of OTC drug products may include a telephone number as a source to answer questions about the product, with the heading "Questions?" or "Questions or comments?" These regulations state that a graphic of a telephone or telephone receiver may appear before the heading, and recommend that the label also include a statement about the days of the week and times of the day when a person is available to respond to questions (21 CFR 201.66(c)(9)).

When a responsible person chooses to provide a domestic phone number (rather than an address) to satisfy the labeling requirement of section 502(x), the responsible person may use the same telephone number described under section 201.66(c)(9) to receive reports of adverse events, assuming that the responsible person has in place the necessary personnel and procedures to receive such reports through this phone number.

Under this approach, if the responsible person decides to provide a clarifying statement to inform consumers that the phone number is for reporting serious adverse events, there are two ways to convey the statement within the "Drug Facts" label:

- Include the statement and phone number within the information described in section 201.66(c)(9), by using one of the required headings (i.e. "Questions?" or "Questions or comments?") and include the statement after the phone number, such as "Serious side effects associated with use of this product may be reported to this number."

- Include the clarifying statement under the "Other Information" heading, described in section 201.66(c)(7), and a reference to the phone number listed under section 201.66(c)(9), such as "Serious side effects associated with use of the product may be reported to the phone number provided below."

Finally, when a responsible person chooses to provide a domestic phone number (rather than address) that is not the same phone number described under section 201.66(c)(9), the phone number should be included either (1) under the "Other Information" heading described in section 201.66(c)(7) or (2) outside of the "Drug Facts" label, such as the location on the label that identifies the manufacturer's "place of business." Under these circumstances, the label may include an introductory statement, such as "Call [phone number] to report serious side effects associated with the use of this product."

Q3: When do the labeling requirements in section 502(x) of the Act become effective?

Under section 1(e)(2) of Public Law 109-460, the labeling requirements of section 502(x) of the Act became effective on December 22, 2007, one year after the date of the law's enactment. We believe that it is reasonable to allow an additional one-year period for firms whose labels do not yet meet the requirements of section 502(x) of the Act to bring their labeling into full compliance. This period of enforcement discretion is consistent with the law's initial length of time provided for compliance and should be adequate to enable all firms to meet the new labeling requirements. Therefore, FDA intends to begin enforcing the labeling requirements of section 502(x) of the Act for OTC drug products marketed without an approved application that are labeled on or after January 1, 2009.