Guidance for Industry

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

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

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Guidance for Industry[1] Labeling of Nonprescription Human Drug Products Marketed Without an Approved Application as Required by the Dietary Supplement and Nonprescription Drug Consumer Protection Act: Questions and Answers

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. 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. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

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) (21 U.S.C. 352(x)). 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 Act, (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.

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

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

[2] Available on the Internet at *http://www.fda.gov/cder/regulatory/default.htm#Legislation*.

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 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 2(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 domestic 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 (e.g., a toll-free area code such as 800 or a local area code such as 301). 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.

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 *domestic address or domestic phone number* means a complete address or phone number (see section 502(x) of the Act). This phrase shows Congress's intent that the domestic address or domestic 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.

[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 without an approved application, including those marketed under the OTC Drug Monograph Review process (whether or not subject to a final monograph) and those marketed outside the monograph system.

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

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 might decide not to submit a report to the responsible person because they believe it will not be received. Similarly, if the phone number provided on the product label for adverse event reporting does not include an area code, there is no assurance that consumers will be able to 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, *place of business* address already required in § 201.1(i) of the regulations 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 phone number or domestic address 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 phone number or domestic address for the responsible person, FDA recommends that the label bear a clear, prominent statement informing consumers that the domestic phone number or domestic address is for reporting serious adverse events associated with use of the product. Such a statement can also be used to clarify that a doctor should be called for medical advice.

As stated in FDA's *Drug Facts* regulations (21 CFR 201.66(c)(9)), 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.

When the responsible person chooses to provide a **domestic phone number** (rather than a domestic address) to satisfy the labeling requirement of section 502(x) of the Act, and if the responsible person decides to provide a clarifying statement, the phone number and clarifying statement can be included in one of the following ways:

- Under the *Questions?* or *Questions or comments?* heading described in 21 CFR 201.66(c)(9). The responsible person can use the same telephone number described in § 201.66(c)(9) for product questions or comments to receive reports of adverse events, assuming that

the responsible person has in place the personnel and procedures to receive such reports through this phone number. With this option, FDA recommends that the responsible person include the clarifying statement after the telephone number to emphasize that the same number may be used for questions, comments or reporting adverse events. For example, "You may also report serious side effects to this phone number." Alternatively, the responsible person can include the clarifying statement under the *Other Information* heading described in § 201.66(c)(7), with a reference to the telephone number under *Questions or Comments?*, such as "You may report serious side effects to the phone number provided under *Questions?* below."

- Under the *Other Information* heading. The responsible person can include a phone number and clarifying statement, such as "You may report serious side effects to *[insert phone number]*."

- The responsible person can include the phone number and clarifying statement outside of *Drug Facts*, such as the location on the label that identifies the manufacturer's *place of business*. For example, "You may report serious side effects to *[insert phone number]*."

When the responsible person chooses to provide a **domestic address** (rather than a domestic 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, 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, FDA recommends that the label include an introductory statement, such as "You may report serious side effects to: [*insert street address or P.O. Box, city, state, and zip code]*."

Responsible persons may provide on the product label an email address or website to which reports may be made, provided that such email address or website is in addition to the domestic phone number or domestic address required by Section 502(x) of the Act.

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

Under section 1(e)(2) of Public Law 109-462, 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. Therefore, these labeling requirements are already in effect. However, this final guidance sets forth FDA's intention to exercise enforcement discretion for the new labeling requirements until January 1, 2010. This period of enforcement discretion should be adequate to enable all firms to meet the 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, 2010.

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

IV. PAPERWORK REDUCTION ACT OF 1995

This guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520).

The time required to complete this information collection is estimated to average of 4 hours per response, including the time to review instructions, search existing data sources, gather the data needed, and complete and review the information collection. Send comments regarding this burden estimate or suggestions for reducing this burden to:

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Silver Spring, MD 20993-0002

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