Guidance for Industry on 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

SUPPORTING STATEMENT

A. Justification

1. Circumstances Making the Collection of Information Necessary

This information collection approval request is for a Food and Drug Administration (FDA) guidance for industry entitled "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."

Public Law 109–462, the Dietary Supplement and Nonprescription Drug Consumer Protection Act, which was signed by the President on December 22, 2006, amends the Federal Food, Drug, and Cosmetic Act (the act) to add safety reporting requirements for nonprescription drug products that are marketed without an approved application. In accordance with section 760(b) of the act (21 U.S.C. 379aa), the manufacturer, packer, or distributor whose name appears on the label of a nonprescription drug marketed in the United States without an approved application (referred to as the responsible person) must submit to FDA any report of a serious adverse event associated with such drug when used in the United States, accompanied by a copy of the label on or within the retail package of such drug. Public Law 109-462 also added section 502(x) of the act (21 U.S.C. 352(x)) to require the label of an nonprescription drug product marketed without an approved application in the United States to include a domestic address or domestic telephone number through which the responsible person may receive a report of a serious adverse event associated with the drug product. If the label does not include the required

domestic address or telephone number, the drug product is misbranded. The guidance provides information on: (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 telephone 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. Public Law 109–462 also requires certain postmarketing safety reports for dietary supplements.

2. Purpose and Use of the Information Collection

In section 760 of the act, Congress has required that important safety information relating to certain nonprescription human drug products be made available to the FDA by manufacturers, packers, or distributors so that it can take appropriate action to protect the public health when necessary.

3. Use of Improved Information Technology and Burden Reduction

FDA has a goal of requiring the submission of mandatory reports in an electronic format. In the *Federal Register* of November 5, 1998 (63 FR 59746), the Agency published an advanced notice of proposed rulemaking to notify drug and biologic manufacturers that it is considering preparing a proposed rule that would require them to submit individual case reports electronically. FDA intends to issue a proposed rule in the near future (see the Unified Agenda of May 6, 2008, RIN 0910-AF96). Many pharmaceutical companies currently are submitting some or all adverse event reports in the Adverse Event Reporting System (AERS) database electronically as specified by at http://www.fda.gov/cder/aerssub/default.htm. In the *Federal*

Register of June 12, 2008, FDA announced the availability of a draft guidance for industry entitled "Providing Regulatory Submissions in Electronic Format—Postmarketing Individual Case Safety Reports." The draft guidance consolidates and revises information in two existing draft guidances pertaining to electronic submission of postmarketing individual case safety reports (ICSRs) and attachments to ICSRs. The submission of ICSRs and ICSR attachments in an electronic format is intended to significantly improve FDA's efficiency in processing, archiving, and reviewing the reports.

4. Efforts to Identify Duplication and Use of Similar Information

The information collection requested under the guidance does not duplicate any other information collection.

5. Impact on Small Businesses or Other Small Entities

Although new drug development is typically an activity completed by large multinational drug firms, the information collection requested under the guidance applies to small as well as large companies. Under the Regulatory Flexibility Act, FDA regularly analyzes regulatory options that would minimize any significant impact on small entities. FDA also assists small businesses in complying with statutory and regulatory requirements. The availability of Form FDA 3500A in a fillable pdf format, at www.fda.gov/medwatch/getforms.htm, facilitates the mandatory reporting efforts to FDA from small businesses.

6. Consequences of Collecting the Information Less Frequently

Less frequent data collection would mean that industry may not make the one-time labeling changes that Congress and FDA believe are necessary to ensure that reports of death, serious injury or illness are received by the manufacturer, packer, distributor, or retailer whose name appears on the label.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

There is no inconsistency with 5 CFR 1320.5. The specific reporting and recordkeeping timeframes are justified by the statutory requirements.

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

In the FEDERAL REGISTER of January 2, 2008 (73 FR 196), FDA published a 60-day notice requesting public comment on the information collection estimates. FDA received one comment on the proposed information collection, stating that the time involved in revising labels would be significantly longer if manufacturers are required to comply by January 1, 2009, as drafted, because the volume of labels required to be revised at one time might exceed labeling revision capacity. Several comments requested that FDA extend the date of its enforcement discretion. In response to comments, on December 11, 2008, FDA published a notice of availability of a revised version of the same draft guidance document (73 FR 75436). The revised draft guidance was identical to the first draft guidance, with the exception that, in the revised draft guidance, FDA stated its intention to exercise enforcement discretion until January 1, 2010. As a result, any label revision made as a result of this guidance would likely be made contemporaneously with other scheduled label revisions, minimizing the burden to industry.

9. Explanation of Any Payment or Gift to Respondents

FDA has not provided and has no intention to provide any payment or gift to respondents under this guidance.

10. Assurance of Confidentiality Provided to Respondents

Section 760(f) of the act provides that a serious adverse report submitted to FDA, including new medical information, under section 760 of the act, or an adverse event report voluntarily submitted to FDA, is considered to be a record about an individual under section 552a of title V of the U.S.C. (commonly referred to as the "Privacy Act of 1974") and a medical or similar file, the disclosure of which would constitute a violation of section 552 of title V (commonly referred to as the "Freedom of Information Act"), not to be disclosed unless all personally identifiable information is redacted. Similarly, 760(h)(2)(B) of the act further protects personally-identifiable information in adverse event reports provided by FDA to any State official.

11. Justification for Sensitive Questions

There are no questions of a sensitive nature.

12. Estimates of Annualized Burden Hours and Costs

Section 502(x) of the act requires the label of a nonprescription drug product marketed without an approved application in the United States to include a domestic address or domestic telephone number through which the responsible person (i.e., the manufacturer, packer,

distributor, or retailer whose name appears on the label) may receive a report of a serious adverse event associated with the product. When the responsible person chooses to provide a domestic address (rather than a telephone number) for adverse event reporting, FDA concluded that the statute requires the product label to bear a full U.S. mailing address that includes the street address or P.O. Box, city, state, and zip code of the responsible person. Similarly, when the responsible person chooses to provide a domestic telephone number for adverse event reporting, FDA concluded that the statute requires the telephone number on the product label to include the area code. Currently, many nonprescription drug products include a domestic telephone number, which is optionally included in the "Drug Facts" label under 21 CFR 201.66(c)(9).

In addition to discussing the statutory requirement that labels include a domestic address or a domestic telephone number, the guidance includes recommendations about the location of this information on the label and the recommendation that the label make clear the purpose of this information.

FDA estimates the burden of this collection of information as follows:

Table 1. -- Estimated One-Time Reporting Burden1

	No. of Respondents	Frequency per Response	Total Responses	Hours Per Response	Total Hours
Domestic address or phone number labeling requirement (21 U.S.C. 502(x)) and recommendation to clarify its purpose	200	500	100,000	4	400,000

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

As indicated in Table 1 of this document, we estimate that approximately 200 manufacturers could revise approximately 100,000 labels to add a full domestic address or a domestic telephone number, and should they choose to adopt the guidance's recommendation, to

add a statement identifying the purpose of the domestic address or telephone number. FDA believes that designing the label change should not take longer than 4 hours per label. Automated printing of the labels should only require a few seconds per label. This estimate accounts for the possibility that every manufacturer will make a label revision, which is unlikely. Because the many nonprescription drug labels currently have a domestic telephone number that satisfies the requirement, we believe some manufacturers will opt not to adopt the guidance's recommendation to add a statement identifying the purpose of the contact address or telephone number, significantly reducing the number of total responses. In addition, because FDA intends to exercise enforcement discretion until January 1, 2010, any label revisions made as a result of this guidance would likely be made contemporaneously with other scheduled label revisions, minimizing the burden to industry. Nonetheless, assuming that all labels are revised, FDA estimates that the total one-time burden for this information collection could be 400,000 hours.

13. Estimates of Other Total Annual Cost Burden to Respondents

FDA typically estimates $4,000 per label or stock-keeping unit (SKU) to make a label revision. If 100,000 labels are revised, the total cost burden to respondents could be $400 million. However, the costs associated with the revisions made as a result of section 502(x) of the act and this guidance would be less if label revisions are made contemporaneously with other scheduled label revisions.

14. Annualized Cost to the Federal Government

Label revisions in response to the guidance are not submitted to FDA for review. Therefore, the only costs to FDA as a result of section 502(x) of the act and this guidance would be the costs

associated with overseeing compliance with the new labeling, which FDA expects to be very small.

15. Explanation for Program Changes or Adjustments

This a new collection.

16. Plans for Tabulation and Publication and Project Time Schedule

There are no publications.

17. Reason(s) Display of OMB Expiration Date is Inappropriate

The agency is not seeking to display the expiration date for OMB approval of the information collection.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification statement identified in Item 19, "Certification for Paperwork Reduction Act Submission," of OMB Form 83-I.