Guidance for Industry on Postmarketing Adverse Event Reporting for Nonprescription Human Drug Products Marketed Without an Approved Application

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 "Postmarketing Adverse Event Reporting for Nonprescription Human Drug Products Marketed Without an Approved Application."

Public Law 109–462, the Dietary Supplement and Nonprescription Drug Consumer Protection Act, which was signed by the President on December 22, 2006, states: "Not later than 270 days after the date of enactment of this Act, the Secretary of Health and Human Services shall issue guidance on the minimum data elements that should be included in a serious adverse event report as described under the amendments made by this Act" (section 2(e)(3)). Public Law 109–462 also requires certain postmarketing safety reports for dietary supplements.

Public Law 109–462 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. In addition, the responsible person must submit followup reports of new medical information related to a submitted serious adverse event report that is received within 1

year of the initial report (section 760(c)(2) of the act). Finally, in accordance with section 760(e) of the act, the responsible person must maintain records related to each report of an adverse event received by the responsible person for a period of 6 years.

In accordance with the statutory mandate, the guidance provides information on: (1) The minimum data elements that should be included in a serious adverse event report; (2) the label that should be included with the report; (3) reporting formats for paper and electronic submissions; and (4) how and where to submit the reports.

2. Purpose and Use of the Information Collection

In section 760 of the act, Congress required that important safety information relating to certain nonprescription drug products be made available to the FDA 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 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

Reports of death, serious injury, or illness are collected only at the frequency that they occur. Less frequent data collection would delay identification of products responsible for

adverse events, including fatalities and permanent injuries. Appropriate FDA action, such as changes in labeling or withdrawal from the market, would be delayed by less frequent reporting.

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 October 15, 2007 (72 FR 58316), FDA published a 60-day notice requesting public comment on the information collection provisions. Seven comments were received related to the guidance document. Upon review of these comments FDA does not plan to revise the information collection.

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

FDA receives approximately 2,500 serious adverse event reports for nonprescription drug products marketed under approved applications, which comprise approximately 20 percent of the overall nonprescription drug market. Based on this data, we estimate between 10,000 and 15,000 (i.e., 12,500) total annual responses from approximately 50 respondents for nonprescription drugs marketed without an approved application, and that each submission will take approximately 2 hours to prepare and submit to FDA.

Table 1. -- Estimated Annual Reporting Burden[1]

	Number of Respondents	Annual Frequency per Response	Total annual Responses	Hours Per Response	Total Hours
Reports of serious adverse drug events (21 U.S.C. 379aa((b) and (c))	50	250	12,500	2	25,000
Total					25,000

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

The guidance also recommends that responsible persons maintain records of efforts to obtain the minimum data elements for a report of a serious adverse drug event and any follow-up reports. Although the guidance document does not provide recommendations on all the recordkeeping activities required under section 760(e) of the act, we are providing an estimate for the burden of this collection. Historically, serious adverse event reports comprise approximately two-thirds, and nonserious adverse event reports comprise approximately one-third, of the total number of postmarketing adverse event reports associated with drugs and biologic therapeutics (except vaccines) received by FDA. Based on this generalization, we estimate the total annual records to be approximately 20,000 records per year, and the number of respondents to be approximately 200. We also estimate that it takes approximately 5 hours to maintain each record.

Table 2. -- Estimated Annual Recordkeeping Burden[1]

	Number of Recordkeepers	Annual Frequency per Recordkeeping	Total Annual Records	Hours per Record	Total Hours
Recordkeep-ing (21 U.S.C. 379aa(e)(1))	200	100	20,000	5	100,000
Total					100,000

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

Therefore, the estimated annual reporting burden for this information collection is 25,000 hours and the estimated annual recordkeeping burden is 100,000 hours.

13. Estimates of Annual Cost Burden to Respondents and Record Keepers

FDA has estimated an average industry wage rate of $50.00 per hour for preparing and submitting the information collection under this guidance. Using the averaged wage rate of

$50.00 per hour, and multiplied times the total hour burden estimated above, the total cost burden to respondents is $6,250,000 (1,250,000 (25,000 x $50) plus $5,000,000 (100,000 x $50).

14. Annualized Cost to the Federal Government

Initial implementation and ongoing administrative activities related to the review of postmarketing adverse event reports for nonprescription human drug products marketed without an approved application include:

• Operating the expanded data systems, including data entry of new reports;

• Maintaining the drug registry for nonprescription drugs;

• Reviewing reports of adverse events;

• Overseeing compliance with new labeling and reporting requirements;

• Inspecting records, assessing fines, and other compliance activities.

FDA estimates the initial implementation costs as related to nonprescription drug products to be $3 million in 2007 and $6 million over the 2007-2011 period. FDA estimates that ongoing administrative costs will be $23 million over the 2008-2001 period. In addition, FDA estimates ongoing costs associated with FDA's enforcement activities will be approximately $500,000 a year, totaling $4 million over the 2010-2016 period.

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 of 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.