Guidance for Industry on Postmarketing Adverse Event Reporting for Medical Products and Dietary Supplements During an Influenza Pandemic

0910-0701

SUPPORTING STATEMENT

Terms of Clearance: None.

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 Medical Products and Dietary Supplements During an Influenza Pandemic." The guidance discusses FDA's intended approach to enforcement of adverse event reporting requirements for drugs, biologics, medical devices, and dietary supplements during an influenza pandemic. FDA anticipates that during an influenza pandemic, industry and FDA workforces may be reduced because of high employee absenteeism, while reporting of adverse events related to widespread use of medical products indicated for the treatment or prevention of influenza may increase. The extent of these possible changes is unknown. The Agency makes recommendations to industry for focusing limited resources on reports related to products indicated for the prevention and treatment of influenza and other specific types of reports indicated in the guidance.

The guidance includes recommendations for planning, notification, and documentation for firms that report postmarketing adverse events. The guidance recommends that each firm's pandemic influenza continuity of operations plan (COOP) include instructions for reporting adverse events, including a plan for the submission of stored reports that were not submitted within regulatory timeframes. The guidance explains that firms that are unable to fulfill normal adverse event reporting requirements during an influenza pandemic should: (1) Maintain documentation of the conditions that prevent them from meeting normal reporting requirements;

(2) notify the appropriate FDA organizational unit responsible for adverse event reporting compliance when the conditions exist and when the reporting process is restored; and (3) maintain records to identify what reports have been stored.

2. Purpose and Use of the Information Collection

FDA believes the approach described in the guidance will make it possible for firms with postmarketing adverse event reporting responsibilities to focus their limited resources on reports related to critical products indicated for the treatment or prevention of influenza. FDA will continue to receive reports on critical medical products. After pre-pandemic conditions are restored, FDA will also have information to ensure that required reports are submitted as part of the Agency's ongoing evaluation of postmarketing adverse events for safety problems.

3. Use of Improved Information Technology and Burden Reduction

Although not specifically addressed in the guidance, we assume that firms will rely on their standard electronic information technology systems to develop and maintain the pandemic influenza COOP recommended in the guidance. We also assume that firms will use standard email technology to notify FDA when normal reporting is not feasible and when the normal reporting processes have been restored.

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

The guidance applies to both large and small firms that are responsible for postmarketing adverse events reporting for drugs, biologics, medical devices, and dietary supplements. 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 regulatory requirements.

6. Consequences of Collecting the Information Less Frequently

We believe that the recommendations in the guidance will help mitigate disruptions in reporting of postmarketing adverse events that may occur as a result in high absenteeism during an influenza pandemic.

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

This guidance contains no inconsistency with the guidelines in 5 CFR 1320.5.

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

In accordance with 5 CFR 1320.8(d), FDA published a 60 day notice for public comment in the FEDERAL REGISTER of August 11, 2014 (79 FR 46839). We received one comment. The comment said that during an influenza pandemic, FDA should not put forth a policy of reduced reporting, especially for newly approved drugs and vaccines. The comment recommended that FDA ask companies to modify their contingency plans by either leveraging the company's remote call-center locations not affected by the pandemic or by outsourcing their safety reporting to such locations. The comment stated that at minimum, FDA should require weekly reporting or establish a threshold number of reports that a company must report to FDA.

The comment added that FDA should specifically require reporting on newly approved drugs or vaccines for which there is little safety information.

FDA Response. The Guidance for Industry on Postmarketing Adverse Event Reporting for Medical Products and Dietary Supplements During an Influenza Pandemic does not describe an approach of reduced reporting during an influenza pandemic. Rather, the guidance states that "normal adverse event reporting processes should be maintained to the maximum extent possible" (see section III.C.1, page 3). FDA also provides recommendations on how to prioritize reporting when regulatory timelines cannot be met due to limited resources during a pandemic, so that FDA continues to receive critical safety information in a timely manner. For example, Table 1 of the guidance outlines how companies should prioritize their submission of postmarketing safety reports during an influenza pandemic if normal processes of mandatory adverse event reporting are not feasible because of high employee absenteeism: Reports for pandemic influenza vaccines, drugs and biological products labeled for the treatment of influenza, drugs and biologics approved for less than three years, and products with special concerns as specified by FDA. The list includes reporting on newly approved products as the comment recommended. The guidance provides resources for companies establishing a continuity of operations (COOP) plan, but specifying the content of the COOP plans as suggested by the comment is beyond the scope of the guidance. Instead, the guidance provides the more general recommendation that "each firm's pandemic influenza COOP plan should include instructions for reporting adverse events and the submission of any stored reports not submitted in the regulatory timeframes" (see section III.B, page 2).

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

Although we do not anticipate any confidentiality issues resulting from the information collection in the guidance, confidentiality of information submitted under marketing applications is protected under 21 CFR 314.430 and 21 CFR part 20. In addition, the unauthorized use or disclosure of trade secrets required in applications is specifically prohibited under section 310(j) of the FD&C Act.

11. Justification for Sensitive Questions

There are no questions of a sensitive nature.

12. Estimates of Annualized Burden Hours

12a. Hour Burden

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

The guidance explains FDA's approach to enforcement of adverse event reporting requirements for drugs, biologics, medical devices, and dietary supplements during an influenza pandemic, including an intent not to object to changes in the timing of submission of certain reports during some stages of the pandemic response. The Agency recommends that each firm's pandemic influenza COOP include instructions for reporting adverse events, including a plan for the submission of stored reports that were not submitted within regulatory timeframes. The draft guidance explains that firms that are unable to fulfill normal adverse event reporting requirements during an influenza pandemic should: (1) Maintain documentation of the conditions that prevent them from meeting normal reporting requirements; (2) notify the appropriate FDA organizational unit responsible for adverse event reporting compliance when

the conditions exist and when the reporting process is restored; and (3) maintain records to identify what reports have been stored.

Based on the number of manufacturers that would be covered by the guidance, we estimate that approximately 5,000 firms will add the following to their COOP: (1) Instructions for reporting adverse events; and (2) a plan for submitting stored reports that were not submitted within regulatory timeframes. We estimate that each firm will take approximately 50 hours to prepare the adverse event reporting plan for its COOP.

We estimate that approximately 500 firms will be unable to fulfill normal adverse event reporting requirements because of conditions caused by an influenza pandemic and that these firms will notify the appropriate FDA organizational unit responsible for adverse event reporting compliance when the conditions exist. Although we do not anticipate such pandemic influenza conditions to occur every year, for purposes of the PRA, we estimate that each of these firms will notify FDA approximately once each year, and that each notification will take approximately 8 hours to prepare and submit.

Concerning the recommendation in the guidance that firms unable to fulfill normal adverse event reporting requirements maintain documentation of the conditions that prevent them from meeting these requirements and also maintain records to identify what adverse event reports have been stored and when the reporting process is restored, we estimate that approximately 500 firms will each need approximately 8 hours to maintain the documentation and that approximately 500 firms will each need approximately 8 hours to maintain the records. Therefore, the total recordkeeping burden that would result from the guidance would be 258,000 hours.

The guidance also refers to previously approved collections of information found in FDA's adverse event reporting requirements in 21 CFR 310.305, 314.80, 314.98, 600.80, 606.170, 640.73, 1271.350, and part 803. These regulations contain collections of information

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) and are approved under OMB control numbers 0910-0116, 0910-0291, 0910-0230, 0910-0308, 0910-0437, and 0910-0543. In addition, the guidance also refers to adverse event reports for nonprescription human drug products marketed without an approved application and dietary supplements required under sections 760 and 761 of the FD&CAct (21 U.S.C. 379aa and 379aa-1), which include collections of information approved under OMB control numbers 0910-0636 and 0910-0635.

Table 1-- Estimated Annual Reporting Burden

Type of Reporting	No. of Respondents	No of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Notify FDA when normal reporting is not feasible	500	1	500	8	4,000

Table 2 -- Estimated Annual Recordkeeping Burden

Type of Recordkeeping	Number of Recordkeepers	Number of Records Per Recordkeeper	Total Annual Records	Average Burden Per Recordkeeper	Total Hours
Add adverse event reporting plan to COOP	5,000	1	5,000	50	250,000
Maintain documentation of influenza pandemic conditions and resultant high absenteeism	500	1	500	8	4,000
Maintain records to identify what reports have been stored and when the reporting process was restored	500	1	500	8	4,000
					258,000

12b. Estimates of Costs

There are one-time labor costs associated with preparing and adding to the COOP a plan for reporting pandemic influenza adverse events. Assuming a loaded wage rate of approximately $85 per hour (averaged from wages for upper management, middle management, and clerical support, plus overhead and personnel benefits), we estimate the one-time costs to be approximately $21,250,000.

There are labor costs associated with maintaining records and notifying FDA of the plan activation and deactivation. Assuming a loaded wage rate of approximately $85 per hour), we estimate these costs to be approximately $1,020,000.

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
Pharmaceutical industry average wage grade for preparing, submitting, and maintaining this information collection	262,000	$85.00	$22,270,000
Total			$22,270,000

13. Estimates of Other Total Annual Cost Burden to Respondents and Recordkeepers

There are no capital, start-up, operating or maintenance costs associated with this information collection.

14. Annualized Cost to the Federal Government

There are 500 total annual responses that may result from this guidance (see table above). FDA estimates that, on average, it would take full-time employees (FTEs) approximately 30 minutes to review each submission. Based on a wage rate of approximately $ 48.00 per hour, we estimate that the Federal costs would be approximately $ 12,000.

15. Explanation for Program Changes or Adjustments

There are no changes or adjustments.

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 not 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.