4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2012-N-0253]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Postmarketing Adverse Drug and Biological Product Experience Reporting and Recordkeeping

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

DATES: Fax written comments on the collection of information by [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: To ensure that comments on the information collection are received, OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, Fax: 202-395-7285, or emailed to oira_submission@omb.eop.gov. All comments should be identified with the OMB control number 0910-0230. Also include the FDA docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Domini Bean, Office of Operations, Food and Drug Administration, Three White Flint North, 10A-12M, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-5733, PRAStaff@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

Postmarketing Adverse Drug and Biological Product Experience Reporting and Recordkeeping

OMB Control Number 0910-0230--Revision

Sections 201, 502, 505, and 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 352, 355, and 371) (FD&C Act) require that marketed drugs be safe and effective. To monitor the safety and efficacy of drugs that are on the market, FDA must be promptly informed of adverse experiences associated with the use of marketed drugs. We have issued regulations at §§ 310.305 and 314.80 (21 CFR 310.305 and 314.80) to implement reporting and recordkeeping requirements that enable us to take necessary action to protect the public health from adverse drug experiences.

All applicants who have received marketing approval of drug products are required to report serious, unexpected adverse drug experiences (15-day "Alert reports"), as well as follow-up reports (§ 314.80(c)(1)). This includes reports of all foreign or domestic adverse experiences as well as those based on information from applicable scientific literature and certain reports from postmarketing studies. Section 314.80(c)(1)(iii) pertains to such reports submitted by nonapplicants.

Under § 314.80(c)(2), applicants must provide periodic reports of adverse drug experiences. A periodic report includes, for the reporting interval, reports of serious, expected adverse drug experiences and all nonserious adverse drug experiences and an index of these reports, a narrative summary and analysis of adverse drug experiences, an analysis of the 15-day Alert reports submitted during the reporting interval, and a history of actions taken because of

adverse drug experiences. Under § 314.80(j), applicants must keep for 10 years records of all adverse drug experience reports known to the applicant.

For marketed prescription drug products without approved new drug applications or abbreviated new drug applications, manufacturers, packers, and distributors are required to report to FDA serious, unexpected adverse drug experiences as well as follow-up reports (§ 310.305(c)). Section 310.305(c)(5) pertains to the submission of follow-up reports to reports forwarded to the manufacturers, packers, and distributors by FDA. Under § 310.305(g), each manufacturer, packer, and distributor shall maintain for 10 years records of all adverse drug experiences required to be reported.

Section 760 of the Act (21 U.S.C. 379aa), also provides for mandatory safety reporting for over-the-counter (OTC) human drug products not subject to applications approved under section 505 of the Act (new drug applications or abbreviated new drug applications). These 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), those marketed outside the monograph system, and including those that have been discontinued from marketing but for which a report of an adverse event was received. Under 21 CFR part 329.100 respondents must submit section 760 reports in an electronic format.

To assist respondents with implementation of section 760 we developed the guidance document entitled "Postmarketing Adverse Event Reporting for Nonprescription Human Drug Products Marketed Without an Approved Application." The guidance document discusses what should be included in a serious adverse drug event report submitted under section 760(b)(1) of

the FD&C Act (21 U.S.C. 379aa(b)(1)), including follow-up reports under 760(c)(2) of the FD&C Act (21 U.S.C. 379aa(c)(2)), and how to submit these reports.

Section 760(e) of the FD&C Act (21 U.S.C. 379aa(e)) also requires that responsible persons maintain records of nonprescription adverse event reports, whether or not the event is serious, for a period of 6 years. The guidance recommends that respondents maintain records of efforts to obtain the minimum data elements for a report of a serious adverse drug event and any follow-up reports. The information collection associated with the guidance is currently approved under OMB Control No. 0910-0636, however we are now consolidating it into this collection.

The primary purpose of FDA's adverse drug experience reporting system is to enable identification of signals for potentially serious safety problems with marketed drugs. Although premarket testing discloses a general safety profile of a new drug's comparatively common adverse effects, the larger and more diverse patient populations exposed to the marketed drug provide the opportunity to collect information on rare, latent, and long-term effects. Signals are obtained from a variety of sources, including reports from patients, treating physicians, foreign regulatory agencies, and clinical investigators. Information derived from the adverse drug experience reporting system contributes directly to increased public health protection because the information enables us to make important changes to the product's labeling (such as adding a new warning), to make decisions about risk evaluation and mitigation strategies or the need for postmarketing studies or clinical trials, and when necessary, to initiate removal of a drug from the market.

In the *Federal Register* of July 11, 2018 (83 FR 32132) we published a 60-day notice requesting public comment on the proposed collection of information approved under OMB Control No. 0910-0230. One comment from an anonymous source referred us to attachments

that were not successfully transmitted. We are therefore unable to address this comment. In the *Federal Register* of August 15, 2018 (83 FR 40520) we published a 60-day notice requesting public comment on the collection of information approved under OMB Control No 0910-0636. No comments were received.

Respondents to the collection of information are manufacturers, packers, distributors, and applicants of FDA-regulated drug and biological products. The following estimates are based on our knowledge of adverse drug experience reporting, including the time needed to prepare the reports and the number of reports submitted to the Agency.

We estimate the burden of this collection of information as follows:

Table 1.--Estimated Annual Reporting Burden[1,2]

21 CFR Section	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
310.305(c)(5)	3	1	3	1	3
314.80(c)(1)(iii)	5	1	5	1	5
314.80(c)(2)	810	17.19	13,923.90	60	835,434
Reports of serious adverse drug events (21 U.S.C. 379aa((b) and (c))	283	687.099	194,449	6	1,166,694
Total					2,002,136

[1] The reporting burden for § 310.305(c)(1), (2), and (3), and § 314.80(c)(1)(i) and (ii) is covered under OMB control number 0910-0645.
[2] The capital costs or operating and maintenance costs associated with this collection of information are approximately $25,000 annually.

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

21 CFR Section	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
310.305(g)	25	1	25	16	400
314.80(j)	352	1,870	658,240	16	10,531,840
Recordkeeping (21 U.S.C. 379aa(e)(1))	300	885.6667	265,700	8	2,125,600

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

21 CFR Section	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
Total					12,657,840

[1] There are no capital costs or operating costs associated with this collection of information.
[2.] There are maintenance costs of approximately $22,000 annually.

Based on submissions received we have increased our burden estimate for reporting under part 314.80(c)(2) and recordkeeping under part 314.80(j). Additionally, and as previously stated, we are consolidating burden associated with reporting and recordkeeping under section 760 of the FD&C Act. Based on our records, we received 194,449 total annual reports from approximately 283 respondents for nonprescription drugs marketed without an approved application. We estimate each submission takes approximately 6 hours to prepare and submit. We estimate that there are 265,700 records per year maintained by approximately 300 respondents, and that it takes 8 hours to maintain each record.

Dated: November 2, 2018.

Leslie Kux,

Associate Commissioner for Policy.

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