4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2018-N-4131]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Food and Drug Administration Adverse Event Reports; Electronic Submissions

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) 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 0910-0645. 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.

FDA Adverse Event Reports; Electronic Submissions--21 CFR 310.305, 314.80, 314.98, 314.540, 329.100, 514.80, 600.80, 1271.350, and Part 803

OMB Control Number 0910-0645--Extension

I. Background

The Safety Reporting Portal (SRP) and the Electronic Submission Gateway (ESG) are the Agency's electronic systems for collecting, submitting, and processing adverse event reports, product problem reports, and other safety information for FDA-regulated products. To ensure the safety and identify any risks, harms, or other dangers to health for all FDA-regulated human and animal products, the Agency needs to be informed whenever an adverse event, product quality problem, or product use error occurs. This risk identification process is the first necessary step that allows the Agency to gather the information necessary to be able to evaluate the risk associated with the product and take whatever action is necessary to mitigate or eliminate the public's exposure to the risk.

Some adverse event reports are required to be submitted to FDA (mandatory reporting) and some adverse event reports are submitted voluntarily (voluntary reporting). Requirements regarding mandatory reporting of adverse events or product problems have been codified in 21 CFR parts 310, 314, 329, 514, 600, 803, and 1271, specifically §§ 310.305, 314.80, 314.98, 314.540, 329.100, 514.80, 600.80, 803.30, 803.40, 803.50, 803.53, 803.56, and 1271.350(a) (21

CFR 310.305, 314.80, 314.98, 314.540, 329.100, 514.80, 600.80, 803.30, 803.40, 803.50, 803.53, 803.56, and 1271.350(a)). While adverse event reports submitted to FDA in paper format using Forms FDA 3500, 3500A, 1932, and 1932a are approved under OMB control numbers 0910-0284 and 0910-0291, this notice solicits comments on adverse event reports filed electronically via the SRP and the ESG, and currently approved under OMB control number 0910-0645.

II. The FDA Safety Reporting Portal Rational Questionnaires

FDA currently has OMB approval to receive several types of adverse event reports electronically via the SRP using rational questionnaires. In this notice, FDA seeks comments on the extension of OMB approval for the following rational questionnaires and the proposed revision of the existing rational questionnaire for tobacco products.

A. Reportable Food Registry Reports

The Food and Drug Administration Amendments Act of 2007 (Pub. L. 110-085) (FDAAA) amended the Federal Food, Drug, and Cosmetic Act (FD&C Act) by creating section 417 (21 U.S.C. 350f), Reportable Food Registry (RFR). Section 417 of the FD&C Act defines "reportable food" as an article of food (other than infant formula or dietary supplements) for which there is a "reasonable probability that the use of, or exposure to, such article of food will cause serious adverse health consequences or death to humans or animals." (See section 417(a)(2) of the FD&C Act.) We designed the RFR report rational questionnaire to enable us to quickly identify, track, and remove from commerce an article of food (other than infant formula and dietary supplements) for which there is a reasonable probability that the use of, or exposure to, such article of food will cause serious adverse health consequences or death to humans or animals. FDA's Center for Food Safety and Applied Nutrition uses the information collected to

help ensure that such products are quickly and efficiently removed from the market to prevent foodborne illnesses. The data elements for RFR reports remain unchanged in this request for extension of OMB approval.

B. Reports Concerning Experience With Approved New Animal Drugs

Section 512(l) of the FD&C Act (21 U.S.C. 360b(l)) and § 514.80(b) of FDA's regulations (21 CFR 514.80(b)) require applicants of approved new animal drug applications (NADAs) and approved abbreviated new animal drug applications (ANADAs) to report adverse drug experiences and product/manufacturing defects to the Center for Veterinary Medicine (CVM). This continuous monitoring of approved NADAs and ANADAs affords the primary means by which we obtain information regarding potential problems with the safety and efficacy of marketed approved new animal drugs as well as potential product/manufacturing problems. Postapproval marketing surveillance is important because data previously submitted to FDA may no longer be adequate, as animal drug effects can change over time and less apparent effects may take years to manifest.

To report adverse drug experiences and product/manufacturing defects using the Agency's paper forms, respondents are required to use Form FDA 1932, "Veterinary Adverse Drug Reaction, Lack of Effectiveness, Product Defect Report." Periodic drug experience reports and special drug experience reports must be accompanied by a completed Form FDA 2301, "Transmittal of Periodic Reports and Promotional Material for New Animal Drugs" (see § 514.80(d)). Form FDA 1932a, "Veterinary Adverse Drug Reaction, Lack of Effectiveness or Product Defect Report," allows for voluntary reporting of adverse drug experiences or product/manufacturing defects by veterinarians and the general public. Collection of information

using existing paper Forms FDA 2301, 1932, and 1932a is approved under OMB control number 0910-0284.

Alternatively, however, we encourage respondents to report adverse drug experiences and product/manufacturing defects electronically. The electronic submission data elements to report adverse drug experiences and product/manufacturing defects electronically remain unchanged in this request for extension of OMB approval.

C. Animal Food Adverse Event and Product Problem Reports

Section 1002(b) of FDAAA directed the Secretary of Health and Human Resources to establish an early warning and surveillance system to identify adulteration of the pet food supply and outbreaks of illness associated with pet food. We developed the Pet Food Early Warning System rational questionnaire as a user-friendly data collection tool, as well as a questionnaire for collecting voluntary adverse event reports associated with livestock food. Information collected in these voluntary adverse event reports contribute to CVM's ability to identify adulteration of the livestock food supply and outbreaks of illness associated with livestock food. We use the information collected to help ensure that such products are quickly and efficiently removed from the market to prevent foodborne illnesses. The electronic submission data elements to report adverse events associated with animal food remain unchanged since last OMB review.

D. Voluntary Tobacco Product Adverse Event and Product Problem Reports

Section 909(a) of the FD&C Act (21 U.S.C. 387i(a)) authorizes FDA to establish regulations with respect to mandatory adverse event reports associated with the use of a tobacco product. We collect voluntary adverse event reports associated with the use of tobacco products from interested parties such as healthcare providers, researchers, consumers, and other users of

tobacco products. Information collected in voluntary adverse event reports contributes to FDA's Center for Tobacco Products (CTP's) ability to be informed of, and assess the real consequences of, tobacco product use.

The need for this collection of information derives from our responsibility to obtain current, timely, and policy-relevant information to carry out our statutory functions. CTP has been receiving adverse event and product problem reports through the SRP since January 2014. CTP has developed two voluntary rational questionnaires on the SRP. The first is utilized by consumers and concerned citizens to report tobacco product adverse event or product problems. A second rational questionnaire is used by tobacco product investigators in clinical trials with investigational tobacco products. Both CTP voluntary rational questionnaires capture tobacco-specific adverse event and product problem information from reporting entities such as healthcare providers, researchers, consumers, and other users of tobacco products.

E. Dietary Supplement Adverse Event Reports

The Dietary Supplement and Nonprescription Drug Consumer Protection Act (DSNDCPA) (Pub. L. 109-462, 120 Stat. 3469) amended the FD&C Act with respect to serious adverse event reporting and recordkeeping for dietary supplements and nonprescription drugs marketed without an approved application.

Section 761(b)(1) of the FD&C Act (21 U.S.C. 379aa-1(b)(1)) requires the manufacturer, packer, or distributor whose name (under section 403(e)(1) of the FD&C Act (21 U.S.C. 343(e)(1)) appears on the label of a dietary supplement marketed in the United States to submit to FDA all serious adverse event reports associated with the use of a dietary supplement, accompanied by a copy of the product label. The manufacturer, packer, or distributor of a dietary supplement is required by the DSNDCPA to use the MedWatch form (Form FDA

3500A) when submitting a serious adverse event report to FDA. In addition, under section 761(c)(2) of the FD&C Act, the submitter of the serious adverse event report (referred to in the statute as the "responsible person") is required to submit to FDA a followup report of any related new medical information the responsible person receives within 1 year of the initial report.

As required by section 3(d)(3) of the DSNDCPA, FDA issued guidance to describe the minimum data elements for serious adverse event reports for dietary supplements. The guidance document entitled "Guidance for Industry: Questions and Answers Regarding Adverse Event Reporting and Recordkeeping for Dietary Supplements as Required by the Dietary Supplement and Nonprescription Drug Consumer Protection Act," discusses how, when, and where to submit serious adverse event reports for dietary supplements and followup reports. The guidance also provides FDA's recommendation on records maintenance and access for serious and non-serious adverse event reports and related documents.

Reporting of serious adverse events for dietary supplements to FDA serves as an early warning sign of potential public health issues associated with such products. Without notification of all serious adverse events associated with dietary supplements, FDA would be unable to investigate and followup promptly, which in turn could cause delays in alerting the public when safety problems are found. In addition, the information received provides a reliable mechanism to track patterns of adulteration in food that supports efforts by FDA to target limited inspection resources to protect the public health. FDA uses the information collected to help ensure that such products are quickly and efficiently removed from the market to prevent foodborne illnesses.

Paper mandatory dietary supplement adverse event reports are submitted to FDA on the MedWatch form, Form FDA 3500A, and paper voluntary reports are submitted on Form FDA

3500. Forms FDA 3500 and 3500A are available as fillable pdf forms. Dietary supplement adverse event reports may be electronically submitted to the Agency via the SRP. This method of submission is voluntary. A manufacturer, packer, or distributor of a dietary supplement who is unable to or chooses not to submit reports using the electronic system will still be able to provide their information by paper MedWatch form, Form FDA 3500A (by mail or Fax). There is no change to the mandatory information previously required on the MedWatch form. The electronic submission data elements to report adverse events associated with dietary supplement products remain unchanged in this request for extension of OMB approval.

F. Food, Infant Formula, and Cosmetic Adverse Event Reports

Rational questionnaires have also been developed for submitting adverse event reports for food, infant formula, and cosmetics. The electronic submission data elements to report adverse events associated with food, infant formula, and cosmetics products remain unchanged in this request for extension of OMB approval.

In the *Federal Register* of November 30, 2018 (83 FR 61653), we published a 60-day notice requesting public comment on the proposed collection of information. One general comment was received suggesting the associated forms could be improved but did not include specific problems that might have been encountered. We are appreciative of this comment and continually seek ways to improve the electronic reporting of adverse events associated with FDA-regulated products.

III. Information Collection Burden Estimate

Description of respondents: The respondents to this collection of information include all persons submitting mandatory or voluntary adverse event reports electronically to FDA via the ESG or the SRP regarding FDA-regulated products.

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

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

Activity	FDA Form No.	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Voluntary Adverse Event Report via the SRP (Other than RFR Reports).	3800	1,800	1	1,800	0.6 (36 minutes)	1,080
Mandatory Adverse Event Report via the SRP (Other than RFR Reports).	3800	3,360	1	3,360	1	3,360
Mandatory Adverse Event Report via the ESG (Gateway-to-Gateway transmission).	3800	3,007,000	1	3,007,000	0.6 (36 minutes)	1,804,200
Mandatory and Voluntary RFR Reports via the SRP.	3800	1,260	1	1,260	0.6 (36 minutes)	756
Total						1,809,396

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

Our estimate of the number of respondents and the total annual responses in table 1, Estimated Annual Reporting Burden, is based primarily on mandatory and voluntary adverse event reports electronically submitted to the Agency. The estimated total annual responses are based on initial reports. Followup reports, if any, are not counted as new reports. Based on our experience with adverse event reporting, we assume it takes respondents 0.6 hour to submit a voluntary adverse event report via the SRP, 1 hour to submit a mandatory adverse event report via the SRP, and 0.6 hour to submit a mandatory adverse event report via the ESG (gateway-to-gateway transmission). Both mandatory and voluntary RFR reports must be submitted via the SRP. We assume it takes respondents 0.6 hour to submit an RFR report, whether the submission is mandatory or voluntary.

The burden hours required to complete paper FDA reporting forms (Forms FDA 3500, 3500A, 1932, and 1932a) are reported under OMB control numbers 0910-0284 and 0910-0291. While we do not charge for the use of the ESG, we require respondents to obtain a public key infrastructure certificate in order to set up the account. This can be obtained in-house or

outsourced by purchasing a public key certificate that is valid for 1 year to 3 years. The certificate typically costs from $20 to $30.

Our estimated burden for the information collection reflects an overall increase of 688,547 hours and a corresponding increase of 1,145,763 responses. We attribute this adjustment to an increase in the number of submissions we have received over the last few years.

Dated: May 22, 2019.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

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