DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2011–N–0231]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Adverse Experience Reporting for Licensed Biological Products; and General Records

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA 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: Submit written comments (including recommendations) on the collection of information by March 25, 2021.

ADDRESSES: To ensure that comments on the information collection are received, OMB recommends that written comments be submitted to *https://www.reginfo.gov/public/do/PRAMain.* Find this particular information collection by selecting ''Currently under Review—Open for Public Comments'' or by using the search function. The OMB control number for this information collection is 0910–0308. 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.

Adverse Experience Reporting for Licensed Biological Products and General Records—21 CFR Part 600

OMB Control Number 0910–0308—Extension

Under the Public Health Service Act (42 U.S.C. 262), FDA may only approve a biologics license application for a biological product that is safe, pure, and potent. When a biological product is approved and enters the market, the product is introduced to a larger patient population in settings different from clinical trials. New information generated during the postmarketing period offers further insight into the benefits and risks of the product, and evaluation of this information is important to ensure its safe use. FDA issued its Adverse Experience Reporting System (FAERS) requirements in part 600 (21 CFR part 600) to enable FDA to take actions necessary for the protection of the public health in response to reports of adverse experiences related to licensed biological products. The primary purpose of FAERS is to identify potentially serious safety problems with licensed biological products. Although premarket testing discloses a general safety profile of a biological product's comparatively common adverse effects, the larger and more diverse patient populations exposed to the licensed biological product provides the opportunity to collect information on rare, latent, and long-term effects. In addition, production and/or distribution problems have contaminated biological products in the past.

FAERS reports are obtained from a variety of sources, including manufacturers, patients, physicians, foreign regulatory agencies, and clinical investigators. Identification of new and unexpected safety issues through the analysis of the data in FAERS contributes directly to increased public health protection. For example, evaluation of these safety issues enables FDA to take focused regulatory action. Such action may include, but is not limited to, important changes to the product's labeling (such as adding a new warning), coordination with manufacturers to ensure adequate corrective action is taken, and removal of a biological product from the market when necessary.

Section 600.80(c)(1) requires licensed manufacturers or any person whose name appears on the label of a licensed biological product to report each adverse experience that is both serious and unexpected, whether foreign or domestic, as soon as possible but in no case later than 15 calendar days of initial receipt of the information by the licensed manufacturer. These reports are known as postmarketing 15-day Alert reports. This section also requires licensed manufacturers to submit any followup reports within 15 calendar days of receipt of new information or as requested by FDA, and if additional information is not obtainable, to maintain records of the unsuccessful steps taken to seek additional information. In addition, this section requires that a person who submits an adverse action report to the licensed manufacturer, rather than to FDA, maintain a record of this action.

Section 600.80(e) requires licensed manufacturers to submit a 15-day Alert report for an adverse experience obtained from a postmarketing clinical study only if the licensed manufacturer concludes that there is a reasonable possibility that the product caused the adverse experience.

Section 600.80(c)(2) requires licensed manufacturers to report each adverse experience not reported in a postmarketing 15-day Alert report at quarterly intervals, for 3 years from the date of issuance of the biologics license, and then at annual intervals. The majority of these periodic reports are submitted annually, since a large percentage of currently licensed biological products have been licensed longer than 3 years.

Section 600.80(k) requires licensed manufacturers to maintain for a period of 10 years records of all adverse experiences known to the licensed manufacturer, including raw data and any correspondence relating to the adverse experiences.

Section 600.81 requires licensed manufacturers to submit, at an interval of every 6 months, information about the quantity of the product distributed under the biologics license, including the quantity distributed to distributors. These distribution reports provide FDA with important information about products distributed under biologics licenses, including the quantity, certain lot numbers, labeled date of expiration, the fill lot numbers for the total number of dosage units of each strength or potency distributed (*e.g.,* 50,000 per 10-milliliter vials), and date of release. FDA may require the licensed manufacturer to submit distribution reports under this section at times other than every 6 months.

Under § 600.82(a), an applicant of a biological product or blood and blood component must notify FDA of a permanent discontinuance of manufacture or an interruption in manufacturing or disruption in supply, as applicable. Under §§ 600.80(h)(2) and 600.81(b)(2), a licensed manufacturer may request a temporary waiver for the requirements under §§ 600.80(h)(1) and 600.80(b)(1), respectively. Requests for waivers must be submitted in accordance with § 600.90. Under § 600.90, a licensed manufacturer may submit a waiver request for any requirements that apply to the licensed manufacturer under §§ 600.80 and 600.81. A waiver request submitted under § 600.90 must include supporting documentation.

Manufacturers of biological products for human use must keep records of each step in the manufacture and distribution of a product, including any recalls. These recordkeeping requirements serve preventative and remedial purposes by establishing accountability and traceability in the manufacture and distribution of products. These requirements also enable FDA to perform meaningful inspections.

Section 600.12 requires, among other things, that records be made concurrently with the performance of each step in the manufacture and distribution of products. These records must be retained for no less than 5 years after the records of manufacture have been completed or 6 months after the latest expiration date for the individual product, whichever represents a later date. In addition, under § 600.12, manufacturers must maintain records relating to the sterilization of equipment and supplies, animal necropsy records, and records in cases of divided manufacturing responsibility with respect to a product.

Under § 600.12(b)(2), manufacturers are also required to maintain complete records pertaining to the recall from distribution of any product. Furthermore, 21 CFR 610.18(b) requires, in part, that the results of all periodic tests for verification of cultures and determination of freedom from extraneous organisms be recorded and retained. The recordkeeping requirements for 21 CFR 610.12(g), 610.13(a)(2), 610.18(d), 680.2(f) and 680.3(f) are approved under OMB control number 0910–0139.

Respondents to this collection of information include manufacturers of biological products (including blood and blood components) and any person whose name appears on the label of a licensed biological product. In table 1, the number of respondents is based on the estimated number of manufacturers that are subject to those regulations or that submitted the required information to the Center for Biologics Evaluation and Research and the Center for Drugs Evaluation and Research, FDA, in fiscal year (FY) 2019. Based on information obtained from the FDA's database system, there were 103 manufacturers of biological products. This number excludes those manufacturers who produce Whole Blood, components of Whole Blood, or in-vitro diagnostic licensed products, because of the exemption under § 600.80(m).

The total annual responses are based on the number of submissions received by FDA in FY 2019. There were an estimated 169,334 15-day Alert reports, 184,265 periodic reports, and 789 lot distribution reports submitted to FDA. The number of 15-day Alert reports for postmarketing studies under § 600.80(e) is included in the total number of 15-day Alert reports. FDA received 63 requests from 40 manufacturers for waivers under § 600.90 (including §§ 600.80(h)(2) and 600.81(b)(2)), of which 61 were granted. The hours per response are based on FDA experience. The burden hours required to complete the MedWatch Form (Form FDA 3500A) for § 600.80(c)(1), (e), and (f) are reported under OMB control number 0910–0291.

In the **Federal Register** of September 1, 2020 (85 FR 54385), we published a 60-day notice requesting public comment on the proposed collection of information. One comment was received but was not responsive to the information collection topics solicited.

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

TABLE 1—ESTIMATED ANNUAL REPORTING BURDEN [1]

21 CFR section	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response (in hours)	Total hours
600.80(c)(1), 600.80(d), 600.80(e); postmarketing 15-day Alert reports	103	1,644.02	169,334	1	169,334
600.82; notification of discontinuance or interruption in manufacturing	21	1.67	35	2	70
600.80(c)(2) periodic adverse experience reports (FAERS)	103	1,788.98	184,265	28	5,159,420
600.81; distribution reports	117	6.744	789	1	789
600.80(h)(2), 600.81(b)(2), 600.90; waiver requests	40	1.575	63	1	63
Total	.....	.....	.....	.....	5,329,676

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

In table 2, the number of respondents is based on the number of manufacturers subject to those regulations. Based on information obtained from FDA's database system, there were 212 licensed manufacturers of biological products in FY 2019. However, the number of recordkeepers listed for § 600.12(a) through (e), excluding (b)(2), is estimated to be 109. This number excludes manufacturers of blood and blood components because their burden hours for recordkeeping have been reported under § 606.160 in OMB control number 0910–0116. The total annual records is based on the annual average of lots released in FY 2019 (6,670), number of recalls made (735), and total number of adverse experience reports received (305,951) in FY 2019. The hours per record are based on FDA experience.

TABLE 2—ESTIMATED ANNUAL RECORDKEEPING BURDEN [1]

21 CFR section; activity	Number of recordkeepers	Number of records per recordkeeper	Total annual records	Average burden per recordkeeper (in hours)	Total hours
600.12; [2] maintenance of records	109	61.19	6,670	32	213,440
600.12(b)(2); recall records	212	3.467	735	24	17,640
600.80(c)(1) and 600.80(k); FAERS records	103	3,433	353,599	1	353,599

TABLE 2—ESTIMATED ANNUAL RECORDKEEPING BURDEN [1]—Continued

21 CFR section; activity	Number of recordkeepers	Number of records per recordkeeper	Total annual records	Average burden per recordkeeper (in hours)	Total hours
Total	.....	.....	.....	.....	584,679

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.
[2] The recordkeeping requirements in § 610.18(b) are included in the estimate for § 600.12.

The burden for this information collection has changed since the last OMB approval. The reporting and recordkeeping burden has increased mostly due to an increase in the number of FAERS reports submitted to FDA and the associated recordkeeping with these reports.

Dated: February 16, 2021.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2020–D–2016]

Policy for Testing of Alcohol (Ethanol) and Isopropyl Alcohol for Methanol, Including During the Public Health Emergency (COVID–19); Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a final guidance for industry entitled ''Policy for Testing of Alcohol (Ethanol) and Isopropyl Alcohol for Methanol, Including During the Public Health Emergency (COVID–19).'' This guidance is intended to alert pharmaceutical manufacturers and pharmacists in State-licensed pharmacies or Federal facilities who engage in drug compounding to the potential public health hazard of alcohol (ethyl alcohol or ethanol) or isopropyl alcohol contaminated with or substituted with methanol. FDA is aware of reports of fatal methanol poisoning of consumers who ingested alcohol-based hand sanitizers that were manufactured with methanol or methanol-contaminated ethanol and is concerned that other drug products containing ethanol or isopropyl alcohol (pharmaceutical alcohol), which are widely used active ingredients in a variety of drug products, could be similarly vulnerable to methanol contamination. As the COVID–19 pandemic has increased the demand for hand sanitizer products, the demand for pharmaceutical alcohol as the active ingredient of those products has also increased. The guidance outlines a policy intended to help pharmaceutical manufacturers and pharmacists in State-licensed pharmacies or Federal facilities who engage in drug compounding avoid the use of pharmaceutical alcohol that is contaminated with or substituted with methanol in drug products. Given the public health emergency presented by coronavirus disease 2019 (COVID–19), this guidance document is being implemented without prior public comment because FDA has determined that prior public participation is not feasible or appropriate, but it remains subject to comment in accordance with the Agency's good guidance practices.

DATES: The announcement of the guidance is published in the **Federal Register** on February 23, 2021. The guidance document is immediately in effect, but it remains subject to comment in accordance with the Agency's good guidance practices.

ADDRESSES: You may submit either electronic or written comments on Agency guidances at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: https://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *https://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *https://www.regulations.gov.*
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand Delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2020–D–2016 for ''Policy for Testing of Alcohol (Ethanol) and Isopropyl Alcohol for Methanol, Including During the Public Health Emergency (COVID–19).'' Received comments will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240–402–7500.

- Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on