

UNITED STATES FOOD & DRUG ADMINISTRATION

Adverse Experience Reporting for Licensed Biological  
Products; and General Records

OMB Control No. 0910-0308

SUPPORTING STATEMENT:

**Part A: Justification**

1. Circumstances Making the Collection of Information Necessary

This information collection supports Food and Drug Administration (FDA) regulations. Under the Public Health Service (PHS) 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. Regulations implementing adverse experience reporting (AER) requirements are codified in 21 CFR Part 600 and enable FDA to take actions necessary for the protection of the public health in response to reports of adverse experiences related to biologics licensed under any provision of section 351 of the PHS Act (42 U.S.C 262). Reporting and recordkeeping provisions are found in the regulations.

To assist respondents with the reporting provisions of the information collection, FDA has created both paper-based and electronic forms. Information may be submitted electronically through *MEDWATCH* or the *Vaccine Adverse Experience Reporting System (VAERS)*. AER reports are filed using the MEDWATCH Form FDA-3500A (approved under OMB Control Nos. 0910-0291 and 0910-0645) or the VAERS-1. Both versions of the forms and instructions are available from the internet at:

[MedWatch: The FDA Safety Information and Adverse Event Reporting Program | FDA Vaccine Adverse Event Reporting System \(VAERS\) \(hhs.gov\)](#)

The forms may also be downloaded, completed, and submitted to the agency by mail or fax.

We therefore request OMB extension of OMB approval for the information collection found in 21 CFR Part 600 as discussed in this supporting statement, and the associated collection instruments.

## 2. Purpose and Use of the Information Collection

The primary purpose of FDA's AER system (FAERS) is to identify potentially serious safety problems with licensed biological products, focusing especially on newly licensed products. 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 licensed biological product provides, for the first time, the opportunity to collect information on rare, latent, and long-term effects. AER 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 the FAERS system 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 not be limited to important changes in 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 where necessary.

The recordkeeping provisions under 21 CFR 600.12 require manufacturers of licensed biological products for human use to maintain records of each step in the manufacture and distribution of products. These requirements provide FDA with the necessary information to help ensure the safety, purity, and potency of biological products. The recordkeeping requirements for §§ 610.12(g), 610.13(a)(2), 610.18(d), 680.2(f) and 680.3(f) are approved under OMB Control No. 0910-0139.

The semiannual 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. This allows FDA to estimate more accurately the incidence of a product's adverse effects in relation to the volume of the product distributed.

The 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. Without this information, FDA could not monitor industry procedures and discharge its statutory responsibility for protecting the nation's health.

## 3. Use of Improved Information Technology and Burden Reduction

The regulations prescribe no particular use of information technology, however we believe nearly all respondents will use electronic means to satisfy the reporting elements of the information collection. In addition, section 321 of the *National Childhood Vaccine Injury Act* (NCVIA, Public Law 99-660) specifically provides for the waiver of paperwork reduction in the implementation of this statute.

Under § 600.80(f)(3), a manufacturer may also use an alternative report form provided the format is equivalent to all elements of information specified in the designated forms and the

format is pre-approved by MEDWATCH or FDA.

#### 4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of any duplicative information collection. Although we maintain related ICRs to account for reporting associated with other FDA-regulated products, this information collection specifically accounts for burden associated with reporting applicable to licensed biologic products.

#### 5. Impact on Small Businesses or Other Small Entities

Because of the public health protection provisions, there are no exceptions to the information collection requirements. At the same time, FDA aids small businesses in complying with its requirements through the agency's Regional Small Business Representatives and through the scientific and administrative staffs within the agency. FDA has provided a small Business Guide on the agency's website at:

<http://www.fda.gov/ForIndustry/SmallBusinessAssistance/default.htm>.

#### 6. Consequences of Collecting the Information Less Frequently

Information collection is consistent with statutory requirements under the PHS and the FFDCa, and with existing agency regulations.

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

The licensed manufacturers are required to submit to FDA a 15-day Alert report for each serious and unexpected adverse experience as well as any follow-up reports within 15 calendar days of receipt of new information or as requested by FDA. This requirement enables FDA to promptly investigate and, when necessary, initiate corrective action to protect the public from potential adverse product interactions.

#### 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 September 1, 2020 (85 FR 54385). FDA received one comment from the public. The comment was not responsive to the topics for which comment was solicited, nor did the comment provide any data or explanation that would support revising the burden we attribute to the information collection requirements.

#### 9. Explanation of Any Payment or Gift to Respondents

There are no incentives, payments or gifts associated with this information collection.

10. Assurance of Confidentiality Provided to Respondents

In preparing this supporting statement, we consulted our Privacy Office to ensure appropriate identification and handling of information collected.

This ICR collects personally identifiable information (PII). The PII is submitted via Form FDA 3500 (MedWatch, The FDA Safety Information and Adverse Event Reporting Program), Form FDA 3500A (MedWatch, The FDA Safety Information and Adverse Event Reporting Program, For Use by User-Facilities, Importers, and Manufacturers – Mandatory Reporting), and Form FDA 3500B (MedWatch Consumer Voluntary Reporting). PII submitted via Form FDA 3500 is patient identifier, date of birth, age, gender, ethnicity, race, first name, last name, address, phone number, email address, and country. PII submitted via Form FDA 3500A is patient identifier, age, sex, date of birth, ethnicity, race, first name, last name, address, phone number, and email address. PII submitted via Form FDA 3500B is first name, last name, address, country, telephone number, and email address. This information collection supports regulations implementing adverse experience reporting (AER) requirements as codified in 21 CFR Part 600 and enables FDA to take actions necessary for the protection of the public health in response to reports of adverse experiences related to biologics licensed under any provision of section 351 of the PHS Act (42 U.S.C 262). Through appropriate form and webpage design, FDA limited submission fields and minimized the PII collected to protect the privacy of the individuals.

Under the Freedom of Information Act (FOIA) (5 U.S.C. 552), the public has broad access to government documents. However, FOIA provides certain exemptions from mandatory public disclosure of government records (5 U.S.C. 552(b)(1-9)). FDA will make the fullest possible disclosure of records to the public, consistent with the rights of individuals to privacy, the property rights of persons in trade and confidential commercial or financial information.

11. Justification for Sensitive Questions

The collection of information does not involve sensitive questions.

12. Estimates of Annualized Burden Hours and Costs

*12a. Annualized Hour Burden Estimate*

Table 1 – Estimated Annual Reporting Burden<sup>1</sup>

21 CFR Section; Activity	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response	Total hours
600.80(c)(1) 600.80(d) and 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

21 CFR Section; Activity	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response	Total hours
600.80(c)(2) periodic adverse experience reports	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), and 600.90; waiver requests	40	1.575	63	1	63
Total					5,329,676

<sup>1</sup> There are no capital or operating and maintenance costs associated with the information collection.

Respondents to this collection of information are manufacturers of biological products (including blood and blood components) and any person whose name appears on the label of a licensed biological product. 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 CBER and CDER, FDA, in fiscal year (FY) 2019. Based on information obtained from the FDA's database system, there were 103 manufacturers of licensed biologics. This number excludes those manufacturers who produce Whole Blood or components of Whole Blood and 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 annually 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 FDA3500A) for § 600.80(c)(1), (e), and (f) are reported under OMB Control No. 0910-0291.

Table 2 – Estimated Annual Recordkeeping Burden<sup>1</sup>

21 CFR Section; Activity	No. of recordkeepers	No. of records per recordkeeper	Total annual records	Avg. burden per recordkeeper	Total hours
600.12 <sup>2</sup> ; 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)&600.80(k) AER records	103	3,433	353,599	1	353,599
TOTAL					584,679

<sup>1</sup> There are no capital or operating and maintenance costs associated with the information collection.

<sup>2</sup> The recordkeeping requirements in § 610.18(b) are included in the estimate for § 600.12.

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/approved under § 606.160 in OMB Control No. 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.

*12b. Annualized Cost Burden Estimate*

The estimated annualized cost to the respondents is \$419,469,656.

Cost to Respondents			
Activity	Total Burden Hours	Hourly Wage Rate	Total Respondent Cost
Reporting	5,329,676	\$73	\$389,066,348
Recordkeeping	584,679	\$52	\$30,403,308
TOTAL			\$419,469,656

This cost is based on an average pay rate of \$73.00 per hour for an upper level manager, and mid-level professional that handle the various reporting requirements. This cost is also based on a pay rate of \$52 per hour for a mid-level professional that handles the various recordkeeping requirements. This salary estimate includes benefits but no overhead costs.

13. Estimates of Other Total Annual Costs to Respondents and/or Recordkeepers/Capital Costs

There are no capital costs, operating and maintenance costs associated with this information collection.

14. Annualized Cost to the Federal Government

The estimated total annual cost to FDA is \$127,428,949.

Annual Cost to FDA				
Activity	Number of Reports	Hours per Report	Cost per Hour	Total Cost
Report Distribution	5,329,676	0.1	\$34	\$18,120,898
Report Review	5,329,676	0.33	\$62	\$109,045,171
TOTAL				\$127,166,069

The cost is based on two Regulatory Information Specialists, (GS-9/11), who are responsible for distributing the reports. The cost is also based on a GS-14 Reviewer who is responsible for reviewing the reports. The salaries include benefits but no overhead costs.

Annual Cost to FDA				
Activity	Number of Respondents	Hours per Inspection	Cost per Hour	Total Cost
Inspection	106	40	\$62	\$262,880

There are 212 licensed manufacturers of biological products that will be inspected on a biennial basis. Therefore, it is estimated that approximately one-half (106 establishments) will be inspected annually. The cost estimate is based on a FDA inspector at an average grade of GS-13/5 who takes an average of 40 hours for each establishment to perform the on-site inspection, review the records, and write the report.

15. Explanation for Program Changes or Adjustments

The information collection reflects agency adjustments by an increase of 181,841 burden hours and 95,028 responses annually. We attribute this to an increase in the number of AER reports received by the agency, as well as a greater number of biological products entering the marketplace for which the underlying regulatory requirements apply.

16. Plans for Tabulation and Publication and Project Time Schedule

This information collected will not be published or tabulated.

17. Reason(s) Display of OMB Expiration Date is Inappropriate

FDA is not seeking approval to exempt display of the expiration date for OMB approval.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.