

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

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[Docket No. FDA-2008-N-0073]

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) 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: 202-395-6974, or e-mailed to *baguilar@omb.eop.gov*. All comments should be identified with the OMB control number 0910-0308. Also include the FDA docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Jonna Capezzuto, Office of the Chief Information Officer (HFA-250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-4659.

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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—(OMB Control Number 0910–0308)—Extension

Under the Public Health Service Act (42 U.S.C. 262), FDA is required to ensure the marketing of only those biological products which are safe and effective. FDA must, therefore, be informed of all adverse experiences occasioned by the use of licensed biological products. FDA issued the adverse experience reporting (AER) 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 FDA's AER system is to flag potentially serious safety problems with licensed biological products, focusing especially on newly licensed 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. Reports are obtained from a variety of sources, including patients, physicians, foreign regulatory agencies, and clinical investigators. Information derived from the AER system contributes directly to increased public health protection because such information enables FDA to recommend important changes to the product's labeling (such as adding a new warning), to initiate removal of a biological product from the market when necessary, and to assure the manufacturer has taken adequate corrective action if necessary.

The regulation in § 600.80(c)(1) requires licensed manufacturers 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 are known as postmarketing 15-day Alert reports. Section 600.80(c)(1) also requires licensed manufacturers to submit any followup reports within 15-calendar days of receipt of new information or as requested by FDA.

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 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 will be submitted annually because a large percentage of currently licensed biological products have been licensed longer than 3 years. Section 600.80(i) 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 semiannual distribution reports provide FDA with important information about products distributed under biologics licenses, including the quantity, certain lot numbers, labeled date of expiration, number of dosage units, and date of release. Under § 600.90, a licensed manufacturer may submit a waiver request

for any requirements that applies 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, concurrently with the performance of each step that all records of each step in the manufacture and distribution of a product be made and 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, manufacturers must maintain records of sterilization of equipment and supplies, animal necropsy records, and records in cases of divided manufacturing of a product. Section 600.12(b)(2) requires manufacturers to maintain complete records pertaining to the recall from distribution of any product.

Respondents to this collection of information are manufacturers of biological products. Under table 1 of this document, the number of respondents is based on the estimated number of manufacturers that submitted the required information to the Center for Biologics Evaluation and Research and Center for Drug Evaluation and Research, FDA, in fiscal year (FY) 2006. Based on information obtained from FDA's database system, there were 88 licensed biologics manufacturers. This number excludes those manufacturers who

produce blood and blood components and in-vitro diagnostic licensed products, because § 600.80(k) specifically exempts manufacturers of these products from adverse experience reporting requirements. The total annual responses are based on the estimated number of submissions received annually by FDA in FY 2006. However, not all manufacturers have submissions in a given year and some may have multiple submissions. There were an estimated 23,835 15-day Alert reports, 21,872 periodic reports, and 179 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 6 requests for waiver under § 600.90, all of which were granted. The hours per response are based on FDA experience. The burden hours required to complete the MedWatch Form for § 600.80(c)(1), (e), and (f) are reported under OMB control no. 0910-0291.

In the **Federal Register** of February 15, 2008 (73 FR 8881), FDA published a 60-day notice requesting public comment on the information collection provisions. No comments were received.

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN¹

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
600.80(c)(1) and 600.80(e)	88	270.85	23,835	1	23,835
600.80(c)(2)	88	248.55	21,872	28	612,416
600.81	88	2.03	179	1	179
600.90	6	1	6	1	6
Total					636,436

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

Under table 2 of this document, 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 303 licensed manufacturers of biological products in FY 2006. However, the number of recordkeepers listed for § 600.12(a) through (e) excluding (b)(2) is estimated to be 112. This number

excludes manufacturers of blood and blood components because their burden hours for recordkeeping have been reported under 21 CFR 606.160 in OMB control no. 0910-0116. The total annual records is based on the annual average of lots released (5,291), number of recalls made (1,841), and total number of adverse experience reports received (45,707) in FY 2006. The hours per record are based on FDA experience.

FDA estimates the burden of this recordkeeping as follows:

TABLE 2.—ESTIMATED ANNUAL RECORDKEEPING BURDEN¹

21 CFR Section	No. Of Recordkeepers	Annual Frequency per Recordkeeping	Total Annual Records	Hours per Record	Total Hours
600.12	112	47.24	5,291	32	169,312
600.12(b)(2)	303	6.08	1,841	24	44,184
600.80(i)	88	519.40	45,707	1	45,707
Total					259,203

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

Dated: 5/13/08
May 13, 2008.

Jeffrey Shuren

Jeffrey Shuren,
Associate Commissioner for Policy and Planning.

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