Supporting Statement for
Biological Products: Reporting of Biological Product Deviations in Manufacturing; Forms FDA 3486 and 3486A
OMB# 0910-0458

JUSTIFICATION

1. Need and Legal Basis

The Food and Drug Administration (FDA) is requesting an extension of Office of Management and Budget (OMB) control No. 0910-0458 and OMB approval for the information collection for provisions including Forms FDA 3486 and FDA 3486A (Tab A). The information collection provisions in 21 CFR parts 600 and 606 (Tab B) are listed below:

Section 600.14 (Reporting)-
Requires the licensed manufacturer who holds the biological product license, for other than human blood and blood components, and who had control over the product when the deviation occurred, to report to the Center for Biologics Evaluation and Research (CBER) or to the Center for Drugs Evaluation and research (CDER) as soon as possible but not to exceed 45 calendar days after acquiring information reasonably suggesting that a reportable event has occurred. Form FDA 3486 is required for the submission of these reports.

Section 606.171 (Reporting)-
Requires a licensed manufacturer of human blood and blood components, including Source Plasma; an unlicensed registered blood establishment; or a transfusion service who had control over the product when the deviation occurred, to report to CBER as soon as possible but not to exceed 45 calendar days after acquiring information reasonably suggesting that a reportable event has occurred. Form FDA 3486 is required for the submission of these reports.

Under section 351 of the Public Health Service Act (42 U.S.C. 262) (Tab C), all biological products, including human blood and blood components, offered for sale in interstate commerce must be licensed and meet standards designed to ensure the continued safety, purity, and potency of such products. In addition, the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 351) (Tab D) provides that drugs and devices (including human blood and blood components) are adulterated if they do not conform with current Good Manufacturing Practice (CGMP) assuring that they meet the requirements of the act. All establishments manufacturing human blood and blood components are required to register with FDA, and comply with the current CGMP regulations for human blood and blood components (21 CFR Parts 211, 606, and 820). Transfusion services are required under 42 CFR 493.1271 to comply with 21 CFR Parts 606 and 640 as they pertain to the performance of manufacturing activities. FDA regards biological product deviation reporting to be an essential tool in its directive to protect public health by establishing and maintaining surveillance programs that provide timely and useful information.

2. Information Users

The objectives of the biological product deviation reporting requirement are to: (1) Enable FDA to respond when public health may be at risk; (2) expedite reporting of biological product deviations in manufacturing; (3) provide FDA with uniform data to track trends that may indicate broader threats to the public health; (4) create a uniform reporting requirement that can be enforced against non-complying entities; and (5) help ensure that licensed manufacturers and unlicensed blood establishments are taking appropriate actions to investigate and correct biological product deviations. The reporting system is not intended to overlap quality assurance (QA) programs, but instead builds on those QA programs to assure better protection of the public health. Reporting of biological product deviations will also enable FDA to identify areas in which further regulation or guidance is needed to assist licensed manufacturers and unlicensed blood establishments in decreasing the occurrence of these events.

3. Improved Information Technology

FDA has prepared a standardized form for reporting deviations in the manufacturing of a biological product (BPDR, Form FDA 3486) that may be downloaded from CBER's web site or received by FAX. After completion, the form is sent to the address identified in § 600.14(e). In an effort to expedite and simplify reporting, FDA also provides industry the opportunity to complete and submit the Form FDA 3486 electronically. The establishment may insert the requested information into the appropriate fields on-line and submit the report through CBER's website. The addendum to Form FDA 3486 (Form FDA 3486A) is also web-based and can be submitted electronically.

4. Duplication of Similar Information

In an effort to reduce duplicative reporting, FDA has reviewed other reporting programs. There are two programs that may be misconstrued as being duplicative, but are not duplicative because of their difference in orientation. These two programs are (1) Adverse Experience Reporting for licensed biological products (AER, 21 CFR 600.80) (Tab E), which excludes blood, blood components, and in vitro diagnostic kits, and (2) Medical Device Reporting (MDR, 21 CFR Part 803) (Tab F). Biological product deviation reporting by a firm focuses on the impact deviations in manufacturing have or may have on the safety, purity, and potency of the final product, whereas, AER and MDR reports are focused on the adverse effect of the product on the patient or user.

5. Small Businesses

Although FDA must apply the statutory and regulatory requirements equally to all enterprises, the agency does provide special help to small businesses. CBER's Office of Communication, Training, and Manufacturers Assistance and CDER's Office of Training and Communications provide assistance to small businesses subject to FDA's regulatory requirements.

6. Less Frequent Collection

Less frequent information collection would not provide the information necessary for FDA to monitor the safety, purity, and potency of distributed biological products. Biological product deviation reports, in conjunction with inspections and other surveillance activities, give FDA a continuing overview of the biological product industry. Less frequent collection of information would inhibit FDA's oversight. There are no technical or legal obstacles to reducing the burden.

7. Special Circumstances

The information may be reported to FDA more frequently than quarterly based on the frequency of biological product deviations that may occur during manufacturing.

8. *Federal Register* Notice/Outside Consultation

In accordance with 5 CFR 1320.8(d), on October 31, 2006, in Volume 71, No. 210, page 63772, a 60-day notice for public comment was published in the *Federal Register*. No Comments were received from the public.

9. Payment/Gift to Respondent

FDA has not provided and has no intention to provide any payment or gift to respondents.

10. Confidentiality

The confidentiality of information received by FDA would be consistent with the Freedom of Information Act and the FDA's regulations under 21 CFR Part 20.

11. Sensitive Questions

Questions of a sensitive nature are not applicable to this information collection.

12. Burden Estimate (Total Hours and Wages)

The total annual estimated burden imposed by this collection of information is 86,407 hours.

Estimated Annual Reporting Burden

21 CFR Section	FDA Form Number	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
600.14	3486	147	2.73	401	2.0	802
606.171[1]	3486	194	169.88659	32,958	2.0	65,916
606.171[2]	3486	6,210	1.4993558	9,311	2.0	18,622
	3486A[3]	6,551	0.3255991	2,133	0.5	1,067
Total						86,407

[1] Licensed manufacturers of human blood and blood components, including Source Plasma.
[2] Unlicensed registered blood establishments and transfusion services (1,230+4,980=6,210).
[3] Five percent of the total responses to CBER (42,653x0.05=2,133)

Respondents to this collection of information are the licensed manufacturers of biological products other than human blood and blood components, licensed manufacturers of blood and blood components including Source Plasma, unlicensed registered blood establishments, and transfusion services. Based on information from FDA's database, there are 147 licensed manufacturers of biological products other than human blood and blood components, 194 licensed manufacturers of human blood and blood components, including Source Plasma, and 1,230 unlicensed registered blood establishments. Based on the Center for Medicare and Medicaid Services records, there are an estimated 4,980 transfusion services. The number of licensed manufacturers and total annual responses under § 600.14 include the estimates for both CBER and CDER The number of total annual responses is based on the number of BPD reports FDA received in fiscal year (FY) 2005. The rate of submission is not expected to change significantly in the next few years. Based on information from industry, the estimated average time to complete a deviation report is 2 hours. The availability of the standardized report Form FDA 3486, and the ability to submit this report electronically further streamlines the report submission process.

CBER is developing an addendum to Form FDA 3486. The web-based addendum (Form FDA 3486A) would request additional information when a BPD report has been reviewed by FDA and evaluated as a possible recall. The additional information requested would include information not contained in the Form FDA 3486 such as: (1) Distribution pattern, (2) method of consignee notification, (3) consignee(s) of products for further manufacture, (4) additional product information, and (5) updated product disposition. This information would be requested by CBER through e-mail notification to the submitter of the BPD report. This information would be used by CBER for purposes of recall classification. Form FDA 3486A would be used only for products regulated by CBER. Form FDA 3486A would not be used for the biological products regulated by CDER because they receive very few BPD reports and do not accept electronic filings CBER estimates that 5 percent of the total BPD reports submitted to CBER would need additional information submitted in the addendum. CBER estimates that it would take between 15 to 45 minutes to complete the addendum. For calculation purposes, CBER is using one-half hour.

Activities such as investigating, changing standard operating procedures (SOPs) or processes, and follow-up are currently required under 21 CFR parts 211, (approved under OMB control number 0910-0139, expires September 30, 2008), 606 (approved under OMB control number 0910-0116, expires December 31, 2008), and part 820 (approved under OMB control number 0910-0073, expires September 30, 2007) and, therefore, are not included in the burden calculation for the separate requirement of submitting a deviation report to FDA.

Cost to Respondents

The estimated annualized cost to the respondents is $3,024,245.

Activity	No. of Hours	Cost per Hour	Total Cost
Reporting	86,407	$35	$3,024,245

This estimated cost is based on a pay rate of $35 per hour for a mid-level professional who has the training and skills to handle the various reporting requirements. This salary estimate includes benefits but no overhead costs. There should not be any additional costs of investigating biological product deviations or keeping records of them, since these activities are already required under other sections in 21 CFR Parts 200, 600, and 800.

13. Capitol Costs (Maintenance of Capitol Costs

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

14. Cost to Federal Government

The estimated annualized cost to FDA is $806,445.

Activity	No. of Reports	Hours per Report	Average Cost per Hour	Total Cost
Report Review	44,803	0.4 hr.	$45	$806,445

This estimate is based on a CBER reviewer, at an average pay rate of $45 per hour (GS 13-5), who performs a review and assessment of the report for possible regulatory action. This estimate includes the estimated additional time required to input the data into the database for statistical purposes. The salary estimate includes benefits but no overhead costs.

15. Program or Burden Changes

The previous burden estimate was 67,844 hours. The current overall increase in burden to 86,407 hours is attributed to the increase in the number of annual responses as well as the addition of Form FDA 3486A.

16. Publication and Tabulation Dates

There are no tabulated results to publish for this information collection.

17. Display of OMB Approval Date

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

18. Exceptions to "Certification for Paperwork Reduction Act Submissions"

N/A