Biological Products: Reporting of Biological Product Deviations & Human Cells, Tissues, & Cellular and Tissue-Based Product Deviations; Form FDA 3486 and Addendum 3486A

OMB Control No. 0910-0458

SUPPORTING STATEMENT

Justification

1. Circumstances Making the Collection of Information Necessary

Under section 351 of the Public Health Service Act (PHS Act)(42 U.S.C. 262), all biological products, including human blood and blood components, offered for sale in interstate commerce must be licensed and meet standards, including those prescribed in the FDA regulations, designed to ensure the continued safety, purity, and potency of such products. In addition under section 361 of the PHS Act (42 U.S.C. 264), FDA may issue and enforce regulations necessary to prevent the introduction, transmission, or spread of communicable diseases between the States or possessions or from foreign countries into the States or possessions. Further, section 501 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 351) provides that drugs and devices, including human blood and blood components, are adulterated if they do not conform with Current Good Manufacturing Practice (CGMP). Accordingly, establishments manufacturing biological products including human blood and blood components must comply with the applicable CGMP regulations (Parts 211, 606, and 820 (21 CFR Parts 211, 606, and 820)) and CGTP regulations (21 CFR Part 1271) as appropriate. FDA regards BPD reporting and HCT/P 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. The agency is, therefore, requesting approval for the following provisions:

21 CFR 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 a distributed 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 at a date not to exceed 45 calendar days after acquiring information reasonably suggesting that a reportable event has occurred.

21 CFR 600.171; Reporting

Requires licensed manufacturers of human blood and blood components, including Source Plasma, unlicensed registered blood establishments, or transfusion services who had control over the product when the deviation occurred, to report to CBER as soon as possible but at a date not to exceed 45 calendar days after acquiring information reasonably suggesting that a reportable event has occurred.

21 CFR 1271.350(b); Reporting

Requires human cells, tissues, and cellular and tissue-based product (HCT/P) establishments that manufacture non-reproductive HCT/Ps described in § 1271.10 to investigate and report to CBER all HCT/P deviations relating to a distributed HCT/P that relates to the core current good tissue practice (CGTP) requirements, if the deviation occurred in the establishment's facility or in a facility that performed a manufacturing step for the establishment under contract, agreement, or other arrangement; and to report such HCT/P deviations within 45 days of the discovery of the event.

Forms FDA 3486 and 3486A (*Biological Product Deviation Report* and Web-based Addendum); Reporting

Form FDA 3486 is used to submit biological product deviation (BPD) and HCT/P deviation reports. CBER also developed a Web-based addendum to Form FDA 3486 (Form FDA 3486A) to provide additional information when a BPD report submitted under § 606.171 has been reviewed by FDA and evaluated as a possible recall.

2. Purpose and Use of the Information Collection

The objectives of the BPD reporting and HCT/P deviation reporting requirements are to: (1) enable FDA to respond when public health may be at risk; (2) expedite reporting of BPD and HCT/P 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 as well as manufacturers of HCT/Ps are taking appropriate actions to investigate and correct biological product deviations. The reporting system builds on quality assurance (QA) programs to assure better protection of the public health. Reporting of BPDs and HCT/P deviations also enables FDA to identify areas in which further regulation or guidance is needed to assist licensed manufacturers and unlicensed blood establishments as well as non-reproductive HCT/P establishments in decreasing the occurrence of these events.

3. Use of Improved Information Technology and Burden Reduction

FDA has implemented a standardized form FDA 3486 for reporting deviations in the manufacturing of a biological product. After completion, the form is submitted pursuant to §§ 600.14(e), 606.171(e), or 1271.350(b)(3). Respondents may also submit the information electronically using web-based form FDA 3486A.

4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of duplicative information collection.

5. Impact on Small Businesses or Other Small Entities

The information collection supports agency regulations protecting the public health and provides for no exemptions to small businesses. FDA provides assistance to small businesses through guidance available on our website at: http://www.fda.gov/ForIndustry/SmallBusinessAssistance/SmallBusinessRepresentatives/guidance and through the Center for Biologics Evaluation and Research's (CBER) Office of Communication, Outreach, and Development, Division of Manufacturer's Assistance and Training.

6. Consequences of Collecting the Information Less Frequently

Less frequent information collection would not provide the information necessary for FDA to monitor the safety, purity, and potency of distributed biological products. BPD reports and HCT/P 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 Relating to the Guidelines of 5 CFR 1320.5

The information may be reported to FDA more frequently than quarterly based on the frequency of BPD reports and HCT/P deviation reports that may occur during manufacturing.

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 June 7, 2016 (81 FR 36550). One comment was submitted in response to the notice concerning potential ways to minimize the burden associated with the information collection. The commenter encouraged FDA to permit the use of attachments to Forms FDA 3486 and 3486A when reporting multiple biological product deviations from a single starting source rather than retype the information. The comment suggested, alternatively, that respondents' burden might be reduced by "capping the forms at a much lower number of products/lots than the current maximum of 100." Finally, the comment suggested Forms FDA 3486 and 3486A incorporate technology that would permit barcode scanning for relevant fields.

In our 30-day notice we expressed appreciation of the comment but explained that we are unable to make the suggested revisions to the information collection. Currently, product information can readily be imported from a Microsoft Excel file (in XLS format) into the eBPD report without having to be retyped (up to 100 units/lots). In addition, the product information entered on Form FDA 3486 automatically populates Form FDA 3486A minimizing the need to manually reenter required information. While we will consider future enhancements that allow for attachments and integrates barcode or other technologies that facilitate or otherwise improve reporting, we must ensure that upgrades are compatible with our existing system.

9. Explanation of Any Payment or Gift to Respondents

No payment or gift is provided to respondents.

10. Assurance of Confidentiality Provided to Respondents

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

11. Justification for Sensitive Questions

No questions of a sensitive nature are included in the information collection.

12. Estimates of Annualized Burden Hours and Costs

12a. Annualized Hour Burden Estimate

The estimated annual burden for this information collection is 93,854 hours and 48,930 responses, itemized as follows:

Table 1—Estimate Annual Reporting Burden[1]

21 CFR Section; Activity	FDA Form	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Avg. Burden per Response	Total Hours
600.14; Reporting of BPDs by licensed manufacturers	3486	102	5.99	611	2.0	1,222
606.171; Reporting of product deviations by licensed manufacturers, unlicensed registered blood establishments, and transfusion services	3486	1,738	26.34	45,774	2.0	91,548
1271.350(b); HCT/P deviations	3486	97	2.64	256	2.0	512
Web-based Addendum	3486A[2]	87	26.31	2,289	0.25	572
Total				48,930		93,854

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

[2] Five percent of the number of respondents (1,738 x 0.05 = 87) and total annual responses to CBER (45,774 x 0.05 = 2,289).

12b. Annualized Cost Burden Estimate

The estimated annualized cost to the respondents is $4,035,722, as reflected below:

Activity	Total Burden Hours	Hourly Wage Rate	Total Cost
Reporting	93,854	$43	$4,035,722

This estimated cost is based on a pay rate of $43 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 BPDs and HCT/P deviations or keeping records of them, since these activities are already required under other sections in 21 CFR Parts 211, 606, 820, and 1271.

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

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

14. Annualized Cost to the Federal Government

The estimated annualized cost to FDA is $831,565.35, as reflected below:

Activity	No. of Reports	Time per Report	Average Cost per Hour	Total Cost
Report Review	48,930	~20 minutes (0.33 hours)	$51.50	$831,565.35

This estimate was reached by multiplying the number of annual submissions by the time spent reviewing, assessing, and recording/inputting the information. We then multiplied that figure (161,469) by the average pay rate of $51.50 (GS/13-5 Washington DC/Metro Area) of one FTE.

15. Explanation for Program Changes or Adjustments

The information collection reflects an overall decrease of **18,645** hours and **9,723** responses. We attribute the reduction to a normal variation in submissions of BPDs.

16. Plans for Tabulation and Publication and Project Time Schedule

Information collected will not be tabulated or published.

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

Display of OMB Expiration date is appropriate.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.