UNITED STATES FOOD & DRUG ADMINISTRATION

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

OMB Control No. 0910-0458

SUPPORTING STATEMENT – **Part A: 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 Food and Drug Administration (FDA, the agency, us or we) 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, 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) assuring that they meet the requirements of the FD&C Act. Accordingly, establishments manufacturing biological products including human blood and blood components must comply with the applicable CGMP regulations in 21 CFR Parts 211, 606, and 820, and current good tissue practice (CGTP) regulations (21 CFR Part 1271) as appropriate. We regard Biological Product Deviations (BPD) reporting and human cells, tissues, and cellular and tissue-based product (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.

FDA is, therefore, requesting an extension of Office of Management and Budget (OMB) approval for the information collection associated with the reporting of biological product deviations found in the applicable regulations:

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 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 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.

We are also requesting an extension of OMB approval for associated Form FDA 3486 and Form FDA 3486A (Biological Product Deviation Report and web-based addendum), as discussed in more detail at *Question 3* in this supporting statement.

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 developed the following forms to assist respondents to the information collection:

Forms FDA 3486 and 3486A (*Biological Product Deviation Report* and Web-based Addendum) – Form FDA 3486 is used to submit 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 21 CFR 606.171 has been reviewed by FDA and evaluated as a possible recall. After completion, the form is submitted pursuant to 21 CFR 600.14(e), 606.171(e), or 1271.350(b)(3). Form FDA 3486 can be submitted electronically to CBER, but CDER does not currently accept electronic filings.

Respondents may also submit the information for the web-based Form FDA 3486A electronically.

4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of duplicative information collection. Although FDA has established information collection requests supporting regulations in part 211 (21 CFR 211, currently approved under OMB Control No. 0910-0139); part 600 (21 CFR 600, currently approved under OMB Control No. 0910-0302); and part 1271 (21 CFR 1271, currently approved under OMB Control No. 0910-0543); this information collection specifically supports reporting associated with biological product deviations as described in the applicable regulations and included in our burden analysis at *Question 12*.

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: https://www.fda.gov/industry/small-business-assistance and through the Center for Biologics Evaluation and Research (CBER)'s Office of Communication, Outreach, and Development, Division of Manufacturer's Assistance and Training or Center for Drug Evaluation and Research (CDER)'s Office of Communication.

6. Consequences of Collecting the Information Less Frequently

The information collection schedule is consistent with statutory and regulatory requirements. 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 July 31, 2019 (84 FR 37321). One comment offering general support for the information collection was received in response to the notice.

9. Explanation of Any Payment or Gift to Respondents

No payment or gift is provided to respondents.

10. Assurance of Confidentiality Provided to Respondents

This Information Collection Request collects personally identifiable information (PII) or other data of a personal nature. PII is collected in the context of the subject individuals' professional capacity and the FDA-related work they perform for their employer (e.g., point of contact at a regulated entity). The PII submitted for FDA Form 3486 (Biological Product Deviation Report) is name, telephone number, and email address. The PII submitted for FDA Form 3486A (Addendum) is name, address, telephone number, and email address.

FDA further determined this collection is not subject to the Privacy Act of 1974 and the particular notice and other requirements of the Act do not apply. Specifically, FDA does not use name or any other personal identifier to routinely retrieve records from the information collected.

In preparing this Supporting Statement, FDA staff consulted with the FDA Privacy Office to ensure appropriate handling of information collected. FDA minimized the PII to be collected to protect the privacy of the individuals.

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 94,592.5 hours and 49,328 responses, itemized as follows:

Table 1—Estimate Annual Reporting Burden

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 product deviations by licensed manufacturers	3486	93	6.14	571	2.0	1,142
606.171; Reporting of product deviations by licensed manufacturers, unlicensed registered blood establishments, and transfusion services	3486	1,937	23.847	46,192	2.0	92,384
1271.350(b); HCT/P deviations	3486	93	2.61	243	2.0	486
Form; Web-based Addendum	3486A[1]	102	22.76	2,322	0.25	580.5
Total				49,328		94,592.5

[1] Five percent of the number of respondents (1,937+93 x 0.05 = 102) and total annual responses to CBER (46,192+243 x 0.05 = 2,322).

Activities such as investigating, changing standard operating procedures or processes, and followup are currently required under 21 CFR parts 211 (approved under OMB control number 0910-0139), 606 (approved under OMB control number 0910-0116), 820 (approved under OMB control number 0910-0073). and 1271 (approved under OMB control number 0910-0543) and, therefore, are not included in the burden calculation for the separate requirement of submitting a deviation report to FDA.

12b. Annualized Cost Burden Estimate

The estimated annualized cost to the respondents is $4,256,662.50, as reflected below:

Activity	Total Burden Hours	Hourly Wage Rate	Total Cost
Reporting	94,592.5	$45	$4,256,662.50

This estimated cost is based on a pay rate of $45 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. As stated previously, we estimate no additional costs for 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 $879,024.96, as reflected below:

Activity	No. of Reports	Time per Report	Average Cost per Hour	Total Cost
Report Review	49,328	20 minutes (0.33 hours)	$54.00	$879,024.96

This estimate was reached by multiplying the number of total annual responses by the time spent reviewing and assessing the information. We then multiplied that figure (16,278.24) by the average pay rate of $54.00 (GS/13-5 Washington DC/Metro Area) of one Full-Time Equivalent.

15. Explanation for Program Changes or Adjustments

The information collection reflects an overall increase of 738 hours and 398 responses. We attribute the adjustment to an increase in the number of submissions of BPDs over the last few years. We have also uploaded respondent cost-information to appear at www.reginfo.gov.

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.