UNITED STATES FOOD & DRUG ADMINISTRATION

Current Good Manufacturing Practice (GMP) and Related Regulations for Blood and Blood Components; and Requirements for Donation Testing, Donor Notification, and "*Lookback*"

OMB Control No. 0910-0116 – Revision

SUPPORTING STATEMENT – **Part A: Justification**

Terms of Clearance: We address OMB's terms of clearance in *Question 1*, below.

1. Circumstances Making the Collection of Information Necessary

This information collection supports implementation of Food and Drug Administration (FDA, us or we) regulations and associated guidance. All blood and blood components introduced or delivered for introduction into interstate commerce are subject to section 351(a) of the Public Health Service Act (PHS Act) (42 U.S.C. 262(a)). Section 351(a) of the PHS act requires that manufacturers of biological products, which include blood and blood components intended for further manufacturing into products, have a license, issued upon a demonstration that the product is safe, pure, and potent and that the manufacturing establishment meets all applicable standards, including those prescribed in the FDA regulations designed to ensure the continued safety, purity, and potency of the product. In addition, under section 361 of the PHS Act (42 U.S.C. 264), by delegation from the Secretary of Health and Human Services, FDA may make and enforce regulations necessary to prevent the introduction, transmission, or spread of communicable diseases from foreign countries into the States or possessions, or from one State or possession into any other State or possession.

Section 351(j) of the PHS Act states that the Federal Food, Drug, and Cosmetic (FD&C Act) also applies to biological products. Blood and blood components for transfusion or for further manufacturing into products are drugs, as that term is defined in section 201(g)(1) of the FD&C Act (21 U.S.C. 321(g)(1)). Because blood and blood components are drugs under the FD&C Act, blood and plasma establishments must comply with the provisions and related regulatory scheme of the FD&C Act. For example, under section 501 of the FD&C Act (21 U.S.C. 351), drugs are deemed "*adulterated*" if the methods used in their manufacturing, processing, packing, or holding do not conform to current good manufacturing practice (CGMP) and related regulations.

To implement these statutory provisions, regulations have been codified at 21 CFR part 606 – *Current Good Manufacturing Practice for Blood and Blood Components*; 21 CFR part 610 – *General Biological Products Standards*; 21 CFR part 630 – *Requirements for Blood and Blood Components Intended For Transfusion or For Further Manufacturing Use*; and 21 CFR part 640 – *Additional Standards for Human Blood and Blood Products*. The regulations establish quality standard requirements applicable to blood and blood products including information collection provisions. See Appendix A of this document for a summary list of provisions covered by this information collection.

Description of Respondents: Respondents to this collection of information are licensed and unlicensed blood establishments that collect blood and blood components, including Source Plasma and Source Leukocytes, inspected by FDA, and transfusion services inspected by Centers for Medicare and Medicaid Services (CMS).

ASSOCIATED GUIDANCE:

We revised the information collection to reference the following guidance documents, which were developed consistent with our Good Guidance Practice regulations in 21 CFR part 10.115 that provide for public comment at any time:

The guidance document entitled "*Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion*" (December 2020) provides blood collection establishments and transfusion services with recommendations to control the risk of bacterial contamination of room temperature stored platelets intended for transfusion. The guidance is available for download from our website at: https://www.fda.gov/media/123448/download. The guidance recommends blood collection establishments notify transfusion services if a distributed platelet product is subsequently identified as positive for bacterial contamination and that blood establishments communicate to their consignees the type of storage container the platelets are stored in. We assume such notification is a usual and customary business practice for blood establishments and, therefore, estimate no burden estimate for the information collection.

We also developed the guidance entitled "*Labeling of Red Blood Cell Units with Historical Antigen Typing Results*" (December 2018) to provide establishments that collect blood and blood components for transfusion with recommendations for labeling Red Blood Cell units with non-ABO/Rh(D) antigen typing results obtained from previous donations (historical antigen typing results). Information collection discussed in the guidance is currently approved under OMB control no. 0910-0862. The guidance is available for download from our website at: https://www.fda.gov/media/119376/download. The guidance recommends disclosing non-ABO/Rh(D) historical antigen typing results on a tie-tag or directly on the container label. We assume such disclosures are usual and customary for blood establishments and estimate no burden for the information collection, however for efficiency of agency operations we are consolidating our accounting for the related activities into one information collection.

Accordingly, we request OMB approval of the information collection provisions found in the applicable regulations and associated guidance, as discussed in this supporting statement.

2. Purpose and Use of the Information Collection

The CGMP regulations for human blood and blood components (part 606) and related regulations (parts 610, 630, and 640) implement FDA's statutory authority to ensure the safety, purity, and potency of blood and blood components. The public health objective in testing human blood donations for evidence of relevant transfusion-transmitted infections and in notifying donors is to prevent the transmission of relevant transfusion-transmitted

infections. For example, the "*lookback*" requirements are intended to help ensure the continued safety of the blood supply by providing necessary information to consignees of blood and blood components and appropriate notification of recipients of blood components that are at increased risk for transmitting human immunodeficiency virus (HIV) or hepatitis C virus (HCV) infection.

Consistent with the regulations, records maintained shall be made readily available for authorized inspection. FDA is authorized to inspect these records under section 704 of the FD&C Act (21 U.S.C. 374) (and its enforcement section under section 301(f) of the FD&C Act (21 U.S.C. 331(f)). We use the information to help determine compliance with regulatory requirements established to ensure the safety and efficacy of the covered products. The third-party disclosure requirements identify the various blood and blood components and important properties of the product, demonstrate that the CGMP requirements have been met, and facilitate the tracing of a product back to its original source. The reporting requirements inform FDA of certain information that may require immediate corrective action.

FDA allows the use or shipment prior to test results of human blood or blood components under two circumstances: appropriately documented medical emergency situations or for further manufacturing use as approved in writing by FDA. Use or shipment prior to test results may occur, provided the consignee is notified that test results are not available, the tests for evidence of infection due to relevant transfusion-transmitted infections are performed as soon as possible after release or shipment, and the results are provided promptly to the consignee. The regulations require an establishment to document the emergency release or shipment of blood or blood components prior to completion of testing. If the establishment ships blood or blood components for further manufacturing use prior to completion of testing, the establishment must obtain prior approval from FDA. In either instance, the establishment must complete testing as soon as possible thereafter, and must notify the consignee of test results as soon as they are available. Prior approval is necessary to help ensure that an establishment is following proper procedures in shipping potentially infectious blood and blood components for further manufacturing use. Without this information, FDA could not monitor industry procedures and discharge its statutory responsibility for protecting the nation's health.

The donor notification process is intended to prevent further donations from donors who have been deferred for positive test results for markers of certain relevant transfusion-transmitted infections as prescribed in § 610.41 or for failing to satisfy the donor eligibility criteria under §§ 630.10 and 630.15 prior to collection. Deferred donors are informed of: (1) The reason for the decision; (2) the types of donation that the donor should not donate in the future, if appropriate; (3) the results of the tests for evidence of infection due to relevant transfusion-transmitted infections that were the basis for deferral, if applicable; and (4) information concerning medical follow-up and counseling. By having this information, the deferred donor may make informed decisions as to his or her medical welfare.

3. Use of Improved Information Technology and Burden Reduction

The regulations do not prescribe specific means by which respondents must fulfill the information collection requirements. Establishments may use and we recommend utilization of computer and electronic information technology. Computers may be used for emailing reports to FDA. Notification of consignees can be accomplished by e-mail, phone, fax, or mail. There are no technical obstacles for electronic reporting of the applicable information to FDA. FDA continues to pursue methods of applying technology to reduce burden to the respondents of its information collection as limited resources permit.

4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of duplicative information collection. Although GMP or quality system (QS) regulations appear in several parts of Title 21 (Food and Drugs) of the CFR, this information collection covers provisions applicable to blood and blood products as described under 21 CFR parts 606, 630, and 640 and associated guidance, as discussed in this supporting statement.

5. Impact on Small Businesses or Other Small Entities

The public health protection requirements underlying the information collection apply to all respondents; however, we believe they impose no undue burden on small entities. At the same time, we assist small businesses in complying with agency requirements through CBER's Office of Communication, Outreach and Development (OCOD) and through the scientific and administrative staffs within the agency. We also provide a Small Business Guide on our website at http://www.fda.gov/ForIndustry/SmallBusinessAssistance/default.htm.

6. Consequences of Collecting the Information Less Frequently

The information collection schedule is consistent with statutory and agency requirements established to promote and protect the public health. There are no technical or legal obstacles to reducing the burden.

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

There are no special circumstances associated with this information collection.

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 February 22, 2021 (86 FR 10582). No comments were received in response to the notice.

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. Although personally identifiable information (PII) is collected, it is collected in the context of the subject individuals' professional capacity and the FDA-related work performed for their employer (e.g., point of contact). Specifically, the ICR collects PII in the context of fatality reports; requests for approval to ship or use donations that have a reactive screening tests for a relevant transfusion-transmitted infection; and requests for requalification of deferred donors. Consistent with 21 CFR 606.170(b) PII submitted pertaining to (*Donor or recipient fatality reporting*) includes name, title, telephone number with area code, and fax number (if available), facility's name, mailing address, and FDA registration number (if applicable). Donor information provided can also include name, age and sex of the deceased; date, time, and cause or suspected cause of death (*brief description of event*); and whether an autopsy was or will be performed. Consistent with 21 CFR 610.40(g)(2) (*Application for approval to ship*) PII is submitted with a written application and may include name, address, telephone number, email address and fax number. PII submitted under 610.41(b) (*Request for requalification of a donor*) is contact information submitted with a written request, that might include name, address, telephone number, email address and fax number. PII submitted consistent with 610.40(h)(2)(ii)(A) (*Application for approval for shipment or use*) is contact information submitted with a written application, that might include name, address, telephone number, email address and fax number. PII submitted consistent with 630.35(b) (*Request for requalification of a donor*) is contact information submitted with a written request, that might include name, address, telephone number, email address and fax number. Through appropriate guidance, FDA limited submission fields and minimized the PII collected to protect the privacy of the individuals.

The confidentiality of information received by FDA is consistent with the Freedom of Information Act (FOIA) and FDA's published regulations of "*Public Information*" under 21 CFR part 20. After an FDA investigator completes a routine inspection of a blood or blood component manufacturing establishment, the completed report with the results of the inspection becomes public information, available under the FOIA. However, certain information, such as donor and patient names, for example, is deleted from any information released by FDA under the FOIA and FDA regulations. Manufacturers of human blood and blood components are not required to reveal any proprietary information or trade secrets to achieve compliance with the provisions.

11. Justification for Sensitive Questions

Establishments as part of the donation screening process for blood collection must ask questions of a sensitive nature. These questions are used to evaluate the suitability of a donor. Donors not meeting certain criteria are deferred from donating. This information is necessary to help prevent the transmission of communicable diseases and protect public health. These records are maintained by the establishment and may be reviewed by FDA during an inspection.

12. Estimates of Annualized Burden Hours and Costs

12a. Annualized Hour Burden Estimate

Table 1.--Estimated Annual Reporting Burden[1,2]

21 CFR Section; Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
606.170(b)[2]; Donor or recipient fatality reporting	81	1	81	20	1,620
610.40(g)(2); Application for approval to ship	1	1	1	1	1
610.41(b); Request for requalification of donor	2,653	0.0094	25	7	175
610.40(h)(2)(ii)(A); Application for approval for shipment or use	1	1	1	1	1
630.35(b); Request for requalification of donor	2,653	0.00113	3	7	21
Total					1,818

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

[2] The reporting requirement in § 640.73, which addresses the reporting of fatal donor reactions, is included in the estimate for § 606.170(b).

Table 2 – Estimated Annual Recordkeeping Burden[1]

21 CFR Section; Activity	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
606.100(b)[2]; Maintenance of SOPs	422[5]	1	422	24	10,128
606.100(c); Records of investigations	422[5]	10	4,220	1	4,220
606.110(a)[3]; Documentation donor's health permits plateletpheresis or leukapheresis	43[6]	1	43	0.5 (30 min.)	22
606.151(e); Records of emergency transfusions	422[5]	12	5,064	0.08 (5 min.)	405

21 CFR Section; Activity	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
606.160[4]; Records of collection, processing, compatibility testing, storage, and distribution of each unit of blood and blood components	422[5]	907.583	383,000	0.75 (45 min.)	287,250
606.160(b)(1)(viii); HIV consignee notification	1,789	10.4533	18,701	0.17 (10 min.)	3,179
	4,961	3.6537	18,126	0.17 (10 min.)	3,081
606.160(b)(1)(viii); HCV consignee notification	1,789	22.8060	40,800	0.17 (10 min.)	6,936
	4,961	8.2241	40,800	0.17 (10 min.)	6,936
HIV recipient notification	4,961	0.3538	1,755	0.17 (10 min.)	298
HCV recipient notification	4,961	0.4132	2,050	0.17 (10 min.)	349
606.160(b)(1)(ix); Donor notification records	3,470	757.380	2,628,109	0.05 (3 min.)	131,405
606.160(b)(1)(xi); Physician notification records	1,789	0.2286	409	0.05 (3 min.)	20.5
606.165; Distribution and receipt records	422[5]	907.583	383,000	0.08 (5 min.)	30,640
606.170(a); Adverse reaction records	422[5]	12	5,064	1	5,064
610.40(g)(1); Documentation of medical emergency	3,470	1	3,470	0.5 (30 min.)	1,735
630.15(a)(1)(ii)(B); Documentation required for dedicated donation	1,789	1	1,789	1	1,789
630.20(c); Documentation of exceptional medical need	1,789	1	1,789	1	1,789
Total					495,247

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

[2] The recordkeeping requirements in §§ 606.171, 630.5(d), 630.10(c)(1) and (2), and 640.66, which address the maintenance of SOPs, are included in the estimate for § 606.100(b).

[3] The recordkeeping requirements in § 640.27(b), which address the maintenance of donor health records for the plateletpheresis, are included in the estimate for § 606.110(a).

[4] The recordkeeping requirements in §§ 606.110(a)(2), 630.5(b)(1)(i), 630.10(f)(2) and (4), 630.10(g)(2)(i), 630.15(a)(1)(ii)(A) and (B), 630.15(b)(2), (b)(7)(i)` and (iii), 630.20(a) and (b), 640.21(e)(4), 640.25(b)(4) and (c)(1), 640.31(b), 640.33(b), 640.51(b), 640.53(b) and (c), 640.56(b) and (d), 630.15(b)(2), 640.65(b)(2)(i), 640.65(b)(2)(i), 640.71(b)(1), 640.72, 640.73, and 640.76(a) and (b), which address the maintenance of various records are included in the estimate for § 606.160.

[5] Five percent of establishments that fall under CLIA that transfuse blood and components and FDA-registered blood establishments ($0.05 \times 4,961 + 3,470 = 422$).

[6] Five percent of plateletpheresis and leukapheresis establishments ($0.05 \times 856 = 43$).

Table 3.--Estimated Annual Third-Party Disclosure Burden[1]

21 CFR Section; Activity	No. of Respondents	No. of Disclosures per Respondent	Total Annual Disclosures	Average Burden per Disclosure	Total Hours
606.145(c); Notification of bacterial contamination of platelets	4,961	0.2822	1,400	0.02 (90 seconds)	28
606.170(a); Reports of transfusion reaction	422[2]	12	5,064	0.5 (30 min.)	2,532
610.40(c)(1)(ii); Labeling of donation dedicated to single recipient	3,470	0.0395	137	0.08 (5 min.)	11
610.40(h)(2)(ii)(C) and (D); Labeling of reactive blood and blood components	15	12	180	0.2 (12 min.)	36
610.40(h)(2)(vi); Labeling of reactive blood and blood components	3,470	2.1614	7,500	0.08 (5 min.)	600
610.42(a); Warning statement for medical devices	1	1	1	1	1
610.46(a)(1)(ii)(B); Notification to consignees to quarantine (HIV "lookback")	1,789	5.1984	9,300	0.17 (10 min.)	1,581
610.46(a)(3); Notification to consignees of further testing	1,789	5.1984	9,300	0.17 (10 min.)	1,581
610.46(b)(3); Notification to recipients	4,961	0.3528	1,750	1	1,750
610.47(a)(1)(ii)(B); Notification to consignees to quarantine (HCV "lookback")	1,789	11.4030	20,400	0.17 (10 min.)	3,468
610.47(a)(3); Notification to consignees of further testing	1,789	11.4030	20,400	0.17 (10 min.)	3,468
610.47(b)(3); Notification to recipients	4,961	0.4132	2,050	1	2,050
630.40(a); Notification of donors determined not to be eligible for donation	869	975.834	848,000	0.08 (5 min.)	67,840
630.40(a); Notification of donors deferred based on reactive test results	133	6.323	841	1.5	1,262
630.40(d)(1); Notification to physician of autologous donor	89	2.247	200	1	200
Total					86,408

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

[2] Five percent of establishments that fall under CLIA that transfuse blood and components and FDA-registered blood establishments ($0.05 \times 4,961 + 3,470 = 422$).

Based on current submission data, there are approximately 864 licensed Source Plasma establishments and approximately 1,789 licensed blood collection establishments, for an estimated total of 2,653 (864+1,789). Also, there are an estimated total of 817 unlicensed, registered blood collection establishments for an approximate total of 3,470 collection establishments (864 + 1,789 + 817 = 3,470 establishments). Of these establishments, approximately 856 perform plateletpheresis (777) and leukapheresis (79). These establishments annually collect approximately 73.7 million units of Whole Blood and blood components, including Source Plasma and Source Leukocytes, and are required to follow FDA "lookback" procedures. In addition, there are another estimated 4,961 establishments that fall under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) (formerly referred to as facilities approved for Medicare reimbursement) that transfuse blood and blood components.

Based on available information, we estimate 53.5 million donations of Source Plasma from 2.5 million donors and 12.3 million donations of Whole Blood and apheresis Red Blood Cells, including approximately 10,000 (approximately 0.081 percent of 12.3 million) autologous donations, from approximately 9 million donors. Assuming each autologous donor makes an average of 1.1 donations, we estimate 9,090 autologous donors (10,000 autologous/1.1 average donations). We assume 0.53 percent (56,000/10,654,000) of the 77,000 donations that are donated specifically for the use of an identified recipient are tested under the dedicated donors testing provisions in § 610.40(c)(1)(ii).

Under § 610.40(g)(2) and (h)(2)(ii)(A), Source Leukocytes, a licensed product that is used in the manufacture of interferon, which requires rapid preparation from blood, is currently shipped prior to completion of testing for evidence of infection due to relevant transfusion-transmitted infections. Shipments of Source Leukocytes are approved under a biologics license application and each shipment does not have to be reported to the Agency. Based on information from CBER's database system, FDA receives less than one application per year from manufacturers of Source Leukocytes. However, for calculation purposes, FDA is estimating one application annually.

According our data, there are approximately 15 licensed manufacturers that ship known reactive human blood or blood components under §§ 610.40(h)(2)(ii)(C) and (D). FDA estimates that each manufacturer would ship an estimated 1 unit of human blood or blood components per month (12 per year) that would require two labels; one as reactive for the appropriate screening test under § 610.40(h)(2)(ii)(C), and the other stating the exempted use specifically approved by FDA under § 610.40(h)(2)(ii)(D).

Based on industry feedback, we estimate that 7,500 donations testing reactive by a screening test for syphilis and are determined to be biological false positives by additional testing annually. These units would be labeled accordingly (§ 610.40(h)(2)(vi)). Human blood or a blood component with a reactive screening test, as a component of a medical device, is an integral part of the medical device, e.g., a positive control for an in vitro diagnostic testing kit. It is usual and customary business practice for manufacturers to include on the container label a warning statement that the product was manufactured from a donation found to be reactive for the identified relevant transfusion-transmitted infection(s). In addition, on the rare occasion

when a human blood or blood component with a reactive screening test is the only component available for a medical device that does not require a reactive component, then a warning statement must be affixed to the medical device. To account for this rare occasion under § 610.42(a), we estimate that the warning statement would be necessary no more than once a year.

We estimate that 3,100 repeat donors will test reactive on a screening test for HIV. We assume an average of three components are made from each donation. Under § 610.46(a)(1)(ii)(B) and (a)(3), this estimate results in 9,300 (3,100 x 3) notifications of the HIV screening test results to consignees by collecting establishments for the purpose of quarantining affected blood and blood components, and another 9,300 (3,100 x 3) notifications to consignees of subsequent test results. We assume an average of 10 minutes per notification of consignees is necessary for the information collection.

We estimate 4,961 consignees will be required under § 610.46(b)(3) to notify transfusion recipients, their legal representatives, or physicians of record an average of 0.35 times per year resulting in a total number of 1,755 (585 confirmed positive repeat donors x 3) notifications. Also under § 610.46(b)(3), FDA estimates and includes the time to gather test results and records for each recipient and to accommodate multiple attempts to contact the recipient.

We estimate that 6,800 repeat donors per year would test reactive for antibody to HCV. Under § 610.47(a)(1)(ii)(B) and 610.47(a)(3), collecting establishments would notify the consignee 2 times for each of the 20,400 (6,800 x 3 components) components prepared from these donations, once for quarantine purposes and again with additional HCV test results for a total of 40,800 (2 x 20,400 notifications) notifications as an annual ongoing burden. Under § 610.47(b)(3), we estimate that 4,961 consignees will notify 2,050 recipients or their physicians of record annually.

Based on industry estimates, roughly 18.15 percent of 14,018,000 million potential donors (2,544,000 donors) who come to donate annually are determined ineligible for donation prior to collection. We assume it to be usual and customary business practice for the estimated 2,606 (1,789+817) blood collecting establishments to make notifications onsite and to explain why the donor is determined to be ineligible. Based on available information, we estimate two-thirds (1,737) of the 2,606 blood collecting establishments provided on site additional information and counseling to a donor determined ineligible. Therefore, we estimate that only one-third, or 869 of the 2,606 blood collection establishments would incur burden under § 630.40(a), to provide additional information and counseling to 848,000 (one-third of 2,544,000) ineligible donors.

We assume another 0.6 percent of 14,018,000 donors (84,108 donors) are deferred annually based on test results. We estimate 95 percent of the establishments that collect 99 percent of the blood and blood components notify donors who have reactive test results for HIV, Hepatitis B Virus (HBV), HCV, Human T-Lymphotropic Virus (HTLV), and syphilis as usual and customary business practice. Thus, 5 percent of the 2,653 establishments (133) collecting 1 percent (841) of the deferred donors (84,108) would notify donors under § 630.40(a). We consider it part of usual and customary business practice that collecting

establishments notify an autologous donor's referring physician of reactive test results obtained during the donation process required under § 630.40(d)(1). However, we assume 5 percent of the 1,789 blood collection establishments (89) may not notify the referring physicians of the estimated 2 percent of 10,000 autologous donors with reactive test results (200).

The recordkeeping table reflects the estimate that approximately 95 percent of the recordkeepers, which collect 99 percent of the blood supply, have developed SOPs as part of their customary and usual business practice. Establishments may minimize burdens associated with CGMP and related regulations by using model standards developed by industries' accreditation organizations. These accreditation organizations represent almost all registered blood establishments.

Under § 606.160(b)(1)(ix), we estimate total annual records based on 2,544,000 donors determined ineligible and each of the estimated 2,628,108 (2,544,000 + 84,108) donors deferred based on reactive test results for evidence of infection because of relevant transfusion-transmitted infections. Under § 606.160(b)(1)(xi), only the 1,789 registered blood establishments collect autologous donations and, therefore, are required to notify referring physicians. We estimate 4.5 percent of the 9,090 autologous donors (409) will be deferred under § 610.41 which in turn will lead to the notification of their referring physicians.

Under § 610.41(b), we estimate 25 submissions for requalification of donors and assume there would be only 3 notifications for requalification of donors under § 630.35(b), each requiring 7 hours for submission. FDA permits the shipment of untested or incompletely tested but appropriately documented human blood or blood components in rare medical emergencies and when appropriately documented (§ 610.40(g)(1)). We estimate recordkeeping under § 610.40(g)(1) to be minimal with one or fewer occurrences per year. We consider the reporting of test results to the consignee in § 610.40(g) to be usual and customary business practice of blood establishments. Our assumptions of the average burden per response (hours) and the average burden for recordkeeping (hours) are based on our experience with the collection and informal industry feedback.

The development of labels is a one-time burden. The container labels have been standardized and are sold commercially. The label is only customized for the firm's name and address. In addition, the instruction circular is printed by major blood banking associations, the ARC, AABB, and ABC, and are sold at minimal cost to the firms. The circulars are updated annually usually due to new industry information. Therefore, we assume no burden is incurred as the result of FDA labeling and disclosure regulations (§§ 606.121 and 606.122) and Uniform Labeling of Blood and Blood Components using ISBT 128 (Industry Consensus Standard for the Uniform Labeling of Blood and Blood Components Using ISTB 128.

12b. Annualized Cost Burden Estimate

The estimated annual cost to respondents is $42,593,529.

Activity	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
Reporting	1,818	$73	$132,714
Recordkeeping	495,247	$73	$36,153,031
Disclosure	86,408	$73	$6,307,784
Total			$42,593,529

The cost is based on a pay rate of $48/hour for a medical technologist (MT), who is responsible for recording donor, quarantine, testing, and disposition of information, notifying consignees of test results, and has the training and skills to handle various recordkeeping requirements. The cost estimate is also based on a supervisor, at a pay rate of $65/hour who is responsible for updating SOPs, recording donor information, and notifying physicians of recipients or recipients of test results, investigating, writing, and reporting a fatality, and a Medical Director (MD), at a pay rate of $107/hour, who is responsible for updating SOPs, recording donor information, and notifying physicians of recipients or recipients of test results, investigating, writing, and reporting a fatality. These salary estimates include recordkeeping, reporting, and disclosure requirements that are performed by the MT, supervisor, or MD; the cost/hour includes the average salary of the three ($73). These salary estimates include benefits but no overhead costs.

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

There are no capital, start-up, operating or maintenance costs associated with this information collection.

14. Annualized Cost to the Federal Government

The estimated annualized cost to the Federal Government is $2,836,116. This estimate is based on a FDA reviewer or investigator at an average grade scale of GS-12/5 ($56/hour), who reviews the requests for approval submitted under §§ 610.40(g)(2) and 610.40(h)(2)(ii)(A), or performs biannual on-site inspections. The inspection cost includes inspection of a facility, review of facility records, and report preparation. The cost is based on 1,327 inspections, since the 2,653 facilities are inspected biannually. The estimated cost is also based on a GS-13/5 ($67/hour) Consumer Safety Officer who compiles, reviews, and analyzes fatality reports. In Fiscal Year 2019, FDA received 81 fatality reports. These salary estimates include benefits but no overhead costs.

Activity	Number of Respondents	Number of Hours	Cost per Hour	Total Cost
Product Release Review	2	1	$56	$112
Inspection	1, 237	40	$56	$2,770,880
Fatality Report Review	81	12	$67	$65,124
Total				$2,836,116

15. Explanation for Program Changes or Adjustments

We have adjusted our burden estimate for this information collection since last OMB review to reflect an overall increase of 79,024 hours annually. We attribute this adjustment to an increase in the number of registered blood establishments over the last 3 years. Also, for efficiency of agency operations we have consolidated related information collection approved under 0910-0862 and will discontinue the latter collection upon OMB approval of this request.

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 not display the expiration date for OMB approval.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.

Appendix A

The 0910-0116 information collection includes the following citations:

Citation	Type of Activity	Description
21 CFR 606.100(b) SOPs	Recordkeeping	Requires that written standard operating procedures (SOPs) be maintained for all steps to be followed in the collection, processing, compatibility testing, storage and distribution of blood and blood components used for transfusion and further manufacturing purposes.
21 CFR 606.100(c) SOPs	Recordkeeping	Requires the review of all records pertinent to the lot or unit of blood prior to release or distribution. Any unexplained discrepancy or the failure of a lot or unit of final product to meet any of its specifications must be thoroughly investigated, and the investigation, including conclusions and follow-up, must be recorded.
21 CFR 606.110(a) Records (Donor)	Recordkeeping	Provides that the use of plateletpheresis and leukapheresis procedures to obtain a product for a specific recipient may be at variance with the additional standards for that specific product, if among other things, the physician certifies in writing that the donor's health permits plateletpheresis or leukapheresis.
21 CFR 606.121 Labeling	Disclosure	Requires container label for blood and blood components (except Source Plasma) by all blood establishments.
21 CFR 606.122 Labeling	Disclosure	Requires an instruction circular to provide adequate directions for use, to be available for distribution if the product is intended for transfusion.
21 CFR 606.151(e) SOPs	Recordkeeping	Requires that SOPs for compatibility testing include procedures to expedite transfusion in life-threatening emergencies; records of all such incidents must be maintained, including complete documentation justifying the emergency action, which must be signed by a physician.
21 CFR 606.160 Records (General)	Recordkeeping	Requires that legible and indelible contemporaneous records of each significant step in the collection, processing, compatibility testing, storage, and distribution of each unit of blood and blood components be made so that each unit can be clearly traced and records be maintained for no less than 10 years.
21 CFR 606.160(b)(1)(viii) Records (General)	Recordkeeping	Requires maintenance of records concerning quarantine, notification, testing and disposition performed under the human immunodeficiency virus (HIV) and hepatitis C virus (HCV) ''lookback'' provisions.
21 CFR 606.160(b)(1)(ix) Records (Notification)	Recordkeeping	Requires a blood collection establishment to maintain records of notification of donors deferred or determined not to be eligible for donation, including appropriate follow-up.
21 CFR 606.160(b)(1)(xi) Records (Notification)	Recordkeeping	Requires an establishment to maintain records of notification of the referring physician of a deferred autologous donor, including appropriate follow-up.
21 CFR 606.165 Records	Recordkeeping	Requires that distribution and receipt records be maintained to facilitate recalls, if necessary.
21 CFR 606.170(a) Adverse Reaction Records and Report	Recordkeeping and Disclosure	Requires records to be maintained of any reports of complaints of adverse reactions arising as a result of blood collection or transfusion. Each such report must be thoroughly investigated, and a written report, including conclusions and follow-up, must be prepared and maintained. When an investigation concludes that the product caused the transfusion reaction, copies of all such written reports must be forwarded to and maintained by the manufacturer or collecting facility.
21 CFR 606.170(b) Fatality Report	Reporting	Requires that facilities notify FDA's Center for Biologics Evaluation and Research (CBER) as soon as possible after confirming a complication of blood collection or transfusion to be fatal. The collecting facility is to report donor fatalities, and the compatibility testing facility is to report recipient fatalities. The reporting facility also must submit a written report of the investigation within 7 days after the fatality.
21 CFR 610.40(c)(1)(ii) Labeling	Disclosure	Requires that each donation dedicated to a single identified recipient be labeled as required under § 606.121, and with a label containing the name and identifying information of the recipient.
21 CFR 610.40(g)(1)	Recordkeeping	Requires an establishment to appropriately document a medical emergency for

Records (Medical Emergency)		the release of human blood or blood components prior to completion of required testing.
21 CFR 610.40(g)(2) Approval Request	Reporting	Requires an establishment to obtain written approval from FDA to ship human blood or blood components for further manufacturing use prior to completion of testing for evidence of infection due to certain communicable disease agents.
21 CFR 610.40(h)(2)(ii)(A) Approval Request	Reporting	Requires an establishment to obtain written approval from FDA to use or ship certain human blood or blood components found to be reactive by a screening test for evidence of certain communicable disease agent(s) or collected from a donor with a record of a reactive screening test.
21 CFR 610.40(h)(2)(ii)(C) and (h)(2)(ii)(D) Labeling	Disclosure	Require an establishment to label certain reactive human blood and blood components with the appropriate screening test results, and, if they are intended for further manufacturing use into injectable products, include a statement on the label indicating the exempted use specifically approved by FDA.
21 CFR 610.40(h)(2)(vi) Labeling	Disclosure	Requires each donation of human blood or blood components, excluding Source Plasma, that tests reactive by a screening test for syphilis and is determined to be a biological false positive to be labeled with both test results.
21 CFR 610.42(a) Labeling	Disclosure	Requires a warning statement, "indicating that the product was manufactured from a donation found to be reactive by a screening test for evidence of infection due to the identified communicable agent(s)" in the labeling for medical devices containing human blood or a blood component found to be reactive by a screening test for evidence of infection due to a communicable disease agent(s) or syphilis.
21 CFR 610.46(a)(1)(ii)(B) and 610.47(a)(1)(ii)(B) Consignee Notification	Disclosure	Require a collecting establishment, within 3 calendar days of the donor testing reactive by an HIV or HCV screening test or the collecting establishment becoming aware of other reliable test results or information, to, among other things, notify consignees to quarantine all identified previously collected in-date blood and blood components.
21 CFR 610.46(a)(3) and 610.47(a)(3) Consignee Notification	Disclosure	Require a collecting establishment, within 45 calendar days of the donor testing reactive by an HIV or HCV screening test, to, among other things, notify consignees of supplemental test results, or the results of a reactive screening test if there is no available supplemental test that is approved for such use by FDA.
21 CFR 610.46(b)(3) and 610.47(b)(3) Recipient or Physician Notification	Disclosure	Require consignees to establish, maintain, and follow an appropriate system for performing HIV and HCV ''lookback'' when notified by the collecting establishment that they have received blood and blood components previously collected from donors who later tested reactive for evidence of HIV or HCV infection, or when the collecting establishment is made aware of other reliable test results or information indicating evidence of HIV or HCV infection in a donor. This provision for a system requires the consignee to follow SOPs for, among other things, notifying transfusion recipients of blood and blood components, or the recipient's physician of record or legal representative, when such action is indicated by the results of the supplemental (additional, more specific) tests or a reactive screening test if there is no available supplemental test that is approved for such use by FDA, or if under an investigational new drug application (IND) or an investigational device exemption (IDE), is exempted for such use by FDA. Also, require the consignee to make reasonable attempts to perform the notification within 12 weeks of receipt of the supplemental test result or receipt of a reactive screening test result when there is no available supplemental test that is approved for such use by FDA, or if under an IND or IDE, is exempted for such use by FDA.
21 CFR 630.6(a) Donor Notification	Disclosure	Requires an establishment to make reasonable attempts to notify any donor who has been deferred as required by § 610.41, or who has been determined not to be eligible as a donor.
21 CFR 630.6(d)(1) Physician Notification	Disclosure	Requires an establishment to provide certain information to the referring physician of an autologous donor who is deferred based on the results of tests as described in § 610.41.