Current Good Manufacturing Practices and Related Regulations for Blood and Blood Components; and Requirements for Donor Testing, Donor Notification, and "Lookback"

0910-0116

SUPPORTING STATEMENT

Terms of Clearance: None.

Justification

1. Circumstances Making the Collection of Information Necessary

The Food and Drug Administration (FDA) is requesting an extension of Office of Management and Budget (OMB) Control No. 0910-0116 and OMB approval of the information collection requirements as summarized below:

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)	Recordkeeping	Requires that SOPs for compatibility testing include

SOPs		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) Records (Medical Emergency)	Recordkeeping	Requires an establishment to appropriately document a medical emergency for 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.

In addition to the current good manufacturing practice (CGMP) regulations in part 606 (21 CFR part 606), there are regulations in part 640 (21 CFR part 640) that require additional standards for certain blood and blood components as follows: §§ 640.3(a)(1), (a)(2), and (f); 640.4(a)(1) and (a)(2); 640.25(b)(4) and (c)(1); 640.27(b), 640.31(b), 640.33(b), 640.51(b), 640.53(b) and (c); 640.56(b) and (d); 640.61; 640.63(b)(3), (e)(1), and (e)(3); 640.65(b)(2); 640.66; 640.71(b)(1), 640.72; 640.73; and 640.76(a) and (b). The information collection requirements and estimated burdens for these regulations are included in the part 606 burden estimates, as described in section 12, below.

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). Section 351(a) of the PHS Act requires that manufacturers of biological products, which include blood and blood components intended for further manufacture into injectable 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 manufacture into injectable 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 act, blood and plasma establishments must comply with the substantive 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(a)), drugs are deemed "adulterated" if the methods used in their manufacturing, processing, packing, or holding do not conform to CGMP and related regulations.

The CGMP regulations for human blood and blood components (part 606) and related regulations 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 donors for evidence of infection due to communicable disease agents and in notifying donors is to prevent the transmission of communicable disease. For example, the "lookback" requirements are intended to help ensure the continued safety of the blood supply by providing necessary information to users of blood and blood components and appropriate notification of recipients of transfusion who are at increased risk for transmitting human immunodeficiency virus (HIV) or hepatitis C virus (HCV) infection.

2. Purpose and Use of the Information Collection

The CGMP regulations for human blood and blood components (part 606) and related regulations 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 donors for evidence of infection due to communicable disease agents and in notifying donors is to prevent the transmission of communicable disease. For example, the “lookback" requirements are intended to help ensure the continued safety of the blood supply by providing necessary information to users of blood and blood components and appropriate notification of recipients of transfusion who are at increased risk for transmitting HIV or HCV infection.

The information collection requirements in the CGMP, donor testing, donor notification, and “lookback” regulations provide FDA with the necessary information to perform its duty to ensure the safety, purity, and potency of blood and blood components. These requirements establish accountability and traceability in the processing and handling of blood and blood components and enable FDA to perform meaningful inspections. The recordkeeping requirements serve preventive and remedial purposes. The 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 communicable disease agents 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 communicable disease agents(s) as prescribed in § 610.41 or for failing to satisfy the donor eligibility criteria under §§ 640.3 or 640.63 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 communicable disease agents 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

Establishments may use computers, computer discs, tapes, microfiche, or microfilm in lieu of hard copy records for the purpose of maintaining records. 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.

4. Efforts to Identify Duplication and Use of Similar Information

FDA is the only agency that requires this information. There is no similar information available from any other source.

5. Impact on Small Businesses or Other Small Entities

This collection of information applies to small as well as large facilities. Although FDA must apply the statutory and regulatory requirements to all enterprises, FDA does provide help to small businesses. The Center for Biologics Evaluation and Research (CBER), Office of Communication, Outreach, and Development, Division of Manufacturer's Assistance and Training provides assistance to small businesses concerning FDA's regulatory requirements.

6. Consequences of Collecting the Information Less Frequently

Less frequent information collection would not provide the information necessary for blood establishments to perform the "lookback" procedures, and for FDA to monitor the establishment procedures and ensure the safety of the nation's blood supply. Records are reviewed at the time of inspection for compliance with FDA regulations and for any appropriate corrective action. Initial preparation of SOPs is a one-time burden.

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 for this collection of information.

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 October 20, 2014 (79 FR 62629). FDA received 5 letters of comment. The comments were not responsive to the comment request on the four specified aspects of the

collection of information and did not provide any data or explanation that would support a change regarding the information collection estimates.

9. Explanation of Any Payment or Gift to Respondents

No payment or gift was provided to respondents.

10. Assurance of Confidentiality Provided to Respondents

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 become 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 donor 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

The total annual estimated burden imposed by this collection of information is 510,219 hours.

12a. Annualized Hour Burden Estimate

Table 1. – Estimated Annual Reporting Burden

21 CFR Section	Number of Respondents	Number of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
606.170(b)[1]	72	1	72	20	1,440
610.40(g)(2)	1	1	1	1	1
610.40(h)(2)(ii)(A)	1	1	1	1	1
Total					1,442

[1] 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

21 CFR Section	Number of Recordkeepers	Number of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
606.100(b)[1]	366[4]	1	366	24	8,784
606.100(c)	366[4]	10	3,660	1	3,660
606.110(a)[2]	50[5]	1	50	0.50 (30 minutes)	25
606.151(e)	366[4]	12	4,392	0.08 (5 minutes)	351
606.160[3]	366[4]	1,046.45	383,000	0.75 (45 minutes)	287,250
606.160(b)(1)(viii)					
HIV consignee notification	1,945 4,961	10.80 4.23	21,000 21,000	.17 (10 minutes) .17 (10 minutes)	3,570 3,570
HCV consignee notification	1,945 4,961	24.06 9.43	46,800 46,800	.17 (10 minutes) .17 (10 minutes)	7,956 7,956
HIV recipient notification	4,961	0.35	1,755	.17 (10 minutes)	298
HCV recipient	4,961	0.41	2,050	.17 (10 minutes)	349

notification					
606.160(b)(1)(ix)	2,361	741.21	1,750,000	0.05 (3 minutes)	87,500
606.160(b)(1)(xi)	1,945	2.60	5,063	0.05 (3 minutes)	253
606.165	366[5]	1,046.45	383,000	0.08 (5 minutes)	30,640
606.170(a)	366[5]	12	4,392	1	4,392
610.40(g)(1)	2,361	1	2,361	0.5 (30 minutes)	1,180
Total					447,734

[1] The recordkeeping requirements in §§ 640.3(a)(1), 640.4(a)(1), and 640.66, which address the maintenance of SOPs, are included in the estimate for § 606.100(b).

[2] 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).

[3] The recordkeeping requirements in §§ 640.3(a)(2) and (f); 640.4(a)(2); 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); 640.61; 640.63(b)(3), (e)(1), and (e)(3); 640.65(b)(2); 640.71(b)(1); 640.72; and 640.76(a) and (b), which address the maintenance of various records are included in the estimate for § 606.160.

[4] Five percent of establishments that fall under the Clinical Laboratory Improvement Amendments of 1988 that transfuse blood and components and FDA-registered blood establishments (0.05 x 4,961 + 2,361=366).

[5] Five percent of plateletpheresis and leukopheresis establishments (0.05 x 990=50).

Table 3. – Estimated Annual Third-Party Disclosure Burden

21 CFR Section	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
606.170(a)	366[1]	1.2	439	0.5 (30minutes)	220
610.40(c)(1)(ii)	2,361	1.52	3,600	0.08 (5 minutes)	288
610.40(h)(2)(ii)(C) and (h)(2)(ii)(D)	40	12	480	0.20 (12 minutes)	96
610.40(h)(2)(vi)	2,361	7.62	18,000	0.08 (5 minutes)	1,440
610.42(a)	1	1	1	1	1
610.46(a)(1)(ii)(B)	1,945	5.40	10,500	0.17 (10 minutes)	1,785
610.46(a)(3)	1,945	5.40	10,500	0.17 (10 minutes)	1,785
610.46(b)(3)	4,961	0.35	1,755	1.0	1,755
610.47(a)(1)(ii)(B)	1,945	12.03	23,400	0.17 (10 minutes)	3,978

610.47(a)(3)	1,945	12.03	23,400	0.17 (10 minutes)	3,978
610.47(b)(3)	4,961	0.41	2,050	1.0	2,050
630.6(a)[2]	648	668.72	433,333	0.08 (5 minutes)	34,667
630.6(a)[3]	84	53.57	4,500	1.50 (90 minutes)	6,750
630.6(d)(1)	63	35.71	2,250	1	2,250
Total					61,043

[1] Five percent of establishments that fall under CLIA that transfuse blood and components and FDA-registered blood establishments (0.05 x 4,961 + 2,361=366).

[2] Notification of donors determined not to be eligible for donation based on failure to satisfy eligibility criteria.

[3] Notification of donors deferred based on reactive test results for evidence of infection due to communicable disease agents.

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 other transfusion services inspected by Centers for Medicare and Medicaid Services (CMS). Based on information received from CBER's database systems, there are approximately 416 licensed Source Plasma establishments with multiple locations and approximately 1,265 registered blood collection establishments, for an estimated total of 1,681 establishments. Also, there are an estimated total of 680 unlicensed, registered blood collection establishments for an approximate total of 2,361 collection establishments (416 + 1,265 + 680 = 2,361 establishments). Of these establishments, approximately 990 perform plateletpheresis and leukopheresis. These establishments annually collect approximately 40 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 4,961 establishments that fall under the Clinical Laboratory Improvement Amendments (CLIA) of 1988 (Public Law 100-578) (formerly referred to as facilities approved for Medicare reimbursement) that transfuse blood and blood components.

The reporting, recordkeeping, and disclosure estimates are based on information provided by industry, CMS, and FDA experience. Based on information received from industry, we estimate that there are approximately 25 million donations of Source Plasma from approximately 2 million donors and approximately 15 million donations of Whole Blood, including approximately 225,000 (approximately 1.5% of 15 million) autologous donations, from approximately 10.9 million donors. Assuming each autologous donor makes an average of 2 donations, FDA estimates that there are approximately 112,500 autologous donors.

FDA estimates that approximately 5 percent (3,600) of the 72,000 donations that are donated specifically for the use of an identified recipient would be 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 certain communicable disease agents. Shipments of Source Leukocytes are pre-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, we are estimating one application annually.

Under § 610.40(h)(2)(ii)(C) and (h)(2)(ii)(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). According to CBER's database system, there are approximately 40 licensed manufacturers that ship known reactive human blood or blood components.

Based on information we received from industry, we estimate that approximately 18,000 donations: (1) Annually test reactive by a screening test for syphilis, (2) are determined to be biological false positives by additional testing and (3) are 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 identifies the communicable disease agent. 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.

FDA estimates that approximately 3,500 repeat donors will test reactive on a screening test for HIV. We also estimate that an average of three components was made from each donation. Under § 610.46(a)(1)(ii)(B) and (a)(3), this estimate results in 10,500 (3,500 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 10,500 (3,500 x 3) notifications to consignees of subsequent test results. We estimate an average of 10 minutes per notification of consignees.

We estimate that § 610.46(b)(3) will require 4,961 consignees 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. Under § 610.46(b)(3), we also estimate 1 hour to accommodate the time to gather test results and records for each recipient and to accommodate multiple attempts to contact the recipient.

Furthermore, we estimate that approximately 7,800 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 23,400 (7,800 x 3 components) components prepared from these donations, once for quarantine purposes and again with additional HCV test results for a total of 46,800 notifications as an annual ongoing burden. Under § 610.47(b)(3), we estimate that approximately 4,961 consignees would notify approximately 2,050 recipients or their physicians of record annually. Finally, we estimate 1 hour to complete notification.

Based on industry estimates, roughly 13 percent of 10 million potential donors (1.3 million donors) who come to donate annually are determined not to be eligible for donation prior to collection because of failure to satisfy eligibility criteria. It is the usual and customary business practice of approximately 1,945 (1,265+680) blood collecting establishments to notify onsite and to explain why the donor is determined not to be suitable for donating. Based on such available information, we estimate that two-thirds (1,297) of the 1,945 blood collecting establishments provided on site additional information and counseling to a donor determined not to be eligible for donation as usual and customary business practice. Consequently, we estimate that only one-third, or 648, approximately, blood collection establishments would need to provide, under § 630.6(a), additional information and counseling to the estimated 433,333 (one-third of approximately 1.3 million) ineligible donors.

It is estimated that another 4.5 percent of 10 million donors (450,000 donors) are deferred annually based on test results. We estimate that approximately 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. Consequently, 5 percent of the 1,681 establishments (84) collecting 1 percent (4,500) of the deferred donors (450,000) would notify donors under § 630.6(a).

As part of usual and customary business practice, collecting establishments notify an autologous donor's referring physician of reactive test results obtained during the donation process required under § 630.6(d)(1). However, we estimate that approximately 5 percent of the 1,265 blood collection establishments (63) may not notify the referring physicians of the estimated 2 percent of 112,500 autologous donors with reactive test results (2,250) as their usual and customary business practice.

The recordkeeping chart 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 the total annual records based on the 1.3 million donors determined not to be eligible to donate and each of the estimated 1.75 million (1.3 million + 450,000) donors deferred based on reactive test results for evidence of infection due to communicable disease agents. Under § 606.160(b)(1)(xi), only the 1,945 registered blood establishments collect autologous donations and, therefore, are required to notify referring

physicians. We estimate that 4.5 percent of the 112,500 autologous donors (5,063) will be deferred under § 610.41 and thus result in the notification of their referring physicians.

FDA has concluded that the use of untested or incompletely tested but appropriately documented human blood or blood components in rare medical emergencies should not be prohibited. We estimate the recordkeeping under § 610.40(g)(1) to be minimal with one or fewer occurrences per year. The reporting/disclosure of test results to the consignee in § 610.40(g) does not create a new burden for respondents because it is the usual and customary business practice or procedure to finish the testing and provide the results to the manufacturer responsible for labeling the blood products.

The average burden per response (hours) and the average burden for recordkeeping (hours) are based on estimates received from industry or FDA experience with similar recordkeeping or reporting requirements.

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 no burden is imposed by FDA regarding the 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 Version 3.0.0,March 2013).

12b. Annualized Cost Burden Estimate

The estimated annual cost to respondents is $32,654,016.

Activity	Total Burden Hours	Hourly Wage Rate	Total Respondent Cost
Reporting	1,442	$64	$92,288
Recordkeeping	447,734	$64	$28,654,976
Disclosure	61,043	$64	$3,906,752
Total			$32,654,016

The cost is based on a pay rate of $42/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 $56/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 $92/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 ($64). These salary estimates include benefits but no overhead costs.

13. Estimates of Other Total Annual Cost Burden to Respondents and/or Recordkeepers/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 $1,870,668. This estimate is based on a FDA reviewer or investigator at an average grade scale of GS-12/5 ($54/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 estimated cost is also based on a GS-13/5 ($65/hour) Consumer Safety Officer who compiles, reviews, and analyzes 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	$54	$108
Inspection	840	40	$54	$1,814,400
Fatality Report Review	72	12	$65	$56,160
Total				$1,870,668

15. Explanation for Program Changes or Adjustments

The estimated total annual burden for this information collection was 506,637 hours in 2011. The current increase to 510,219 burden hours (+3,582 hours) is mostly attributed to a slight increase in the number of recordkeepers and corresponding records under § 606.100(b) and (c) and § 606.170(a).

In addition, FDA is consolidating OMB Control No. 0910-0723 into OMB Control No. 0910-0116. There is no change in burden since the burden under 0910-0723 was considered usual and customary practice (§ 606.121).

16. Plans for Tabulation and Publication and Project Time Schedule

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

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

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

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.