FOOD AND DRUG ADMINISTRATION

Donor Risk Assessment Questionnaire for the Food and Drug Administration (FDA)/National Heart, Lung, and Blood Institute (NHLBI)-Sponsored Transfusion-Transmissible Infections Monitoring System (TTIMS)—Risk Factor Elicitation (RFE)

OMB Control No. 0910- NEW

SUPPORTING STATEMENT

Terms of Clearance: None.

A. Justification

1. Circumstances Making the Collection of Information Necessary

The Food and Drug Administration (FDA) is requesting OMB approval of the questionnaire-based information collection discussed below:

TTIMS is a collaboration of the Food and Drug Administration (FDA), National Heart Lung and Blood Institute (NHLBI), Department of Health and Human Services, Office of the Assistant Secretary of Health (HHS/OASH) and large US blood collection systems in the US working together to create a representative, stable, donor hemovigilance program for monitoring current risk factors for transfusion-transmissible infections (TTI) in blood donors using an analytical study design. This capability has been unavailable in the United States until the Transfusion-Transmissible Infection Monitoring System (TTIMS) was established in 2015. Blood establishments participating in TTIMS collect nearly 60% of the nation's blood supply. These include the American Red Cross (ARC), Blood Systems, Inc. (BSI), New York Blood Center (NYBC), and OneBlood.

TTIMS is establishing critical hemovigilance capability for the US through a multi-pronged approach including: 1) The ongoing longitudinal compilation of demographic, donor screening and confirmatory test data that are collected by participating blood centers as part of regulated operational procedures, These data will allow monitoring of the incidence and prevalence of blood donor TTIs; 2) Additional testing of the human immunodeficiency virus (HIV)-positive blood samples that are collected operationally by participating blood centers to better characterize recency of HIV infection; and 3) Monitoring of the distribution of risk factors for HIV and incident HBV and HCV-positive donors who are identified through blood donor screening. The first two TTIMS components have now been established and are supporting incidence and prevalence calculations. The FDA is now requesting OMB approval to allow for the third component of TTIMS to be put into place, namely the collection of information on TTI risk factors among blood donors. This will comprise comprehensive interview-based epidemiological assessment of TTI risk factors and related donor characteristics among seropositive blood donors and controls at the participating blood centers.

Changes to the men who have sex with men (MSM) deferral policy were undertaken by FDA in December, 2015 and fully implemented in December, 2016 with reasonable scientific assurance that blood safety would not be reduced. However, the new donor policy will trigger changes in the donor population. For instance, donors who have not had MSM contact prior to the last 12 months, rather than being deferred indefinitely per the previous policy, are now newly eligible to donate. While the epidemiology and behavioral risks for acquiring HIV and hepatitis B and C infections are known and the uniform donor history questionnaire (DHQ) assesses these risks (e.g. history of MSM, IDU, and sexual contact with an at-risk individual) there remains a need to understand the dynamics and associated factors of donors with TTI risks who proceed with donation despite being ineligible based on current screening criteria. These factors may change in response to external influences, such as the recent change in MSM eligibility.

Previous and Ongoing DHQ Assessments

The current standardized blood donor screening DHQ is based upon known risks for transfusion-transmitted infections and has been developed over the past decade using state of the art epidemiologic information. It has also been assessed for donor cognitive understanding in two separate formal evaluations by the CDC National center for Health Statistics (NCHS). In its current form, it is estimated to be 85-95% effective as a first level screening tool. Despite this success, donors with identifiable risks for HIV and hepatitis continue to present for blood donation. To the extent that such individuals are in the seronegative early stages of infection, they constitute a safety risk to the blood supply.

Recent scientific observations have resulted in development of content elements of the TTIMS risk evaluation instrument that have not previously been studied in blood donors; these include self-perceptions of monogamous behavior, safer sex practices, pre- and post-exposure prophylaxis for HIV, and anti-retroviral therapy. Finally, it is important to recognize that while TTIMS program is focused on blood donation in the US; improved risk screening of potential blood donors is a worldwide concern. Findings from TTIMS and subsequent improvements to blood donor screening and educational measures (and evaluation of these improvements) are likely to improve blood safety internationally.

Standardized Case Interviews

While blood centers generally elicit risk factors when they provide the required counseling to TTI-positive donors, there has not been a systematic or consistent way to elicit or centralize this information on a national level. The TTIMS behavioral risk interviews fill a critical gap by providing a consistent (single instrument), comprehensive, and objective measurement of behavioral risk proportions and related characteristics among donors that potentially influence blood safety.

A recent study by the CDC NCHS reported that some blood donors commonly answer behavioral risk questions at the time of donation based on internal perceptions of whether their blood “is safe” rather than literally answering the actual questions.

The information that can be learned from the TTIMS case donors will allow FDA and blood collection centers to improve the identification and interdiction of similar at-risk individuals in the future. As examples, the TTIMS risk factor assessment will help pinpoint what specific question(s) on the Uniform DHQ might require further evaluation to improve donor attention and the subsequent positive and negative predictive value; and the questionnaire data will also inform the design and evaluation of more effective pre-donation educational materials. In parallel, such improvements in donor screening procedures resulting from TTIMS should also reduce the unnecessary deferral of safe donors.

TTIMS will integrate the risk factor information collected through the blood donor interviews with the demographic and disease marker testing database that has already been established to create a comprehensive hemovigilance safety monitoring database. In this way, the TTIMS program will maintain standardized, statistically and scientifically robust processes for collecting hemovigilance information across blood collection organizations.

Standardized Control Interviews

TTIMS proposes a case-control design to conduct the donor risk factor evaluations and compare time periods. Risk factor information will be captured for prevalent and incident HIV, as well as incident HBV- and HCV-positive donors. It is also important to collect risk factor information on a group of non-infected blood donors to allow for comparisons; TTIMS proposes to use as controls for the risk factor evaluation those donors who have a false-positive screening test. Robust confirmation procedures are used in blood center laboratories to further evaluate the presence of infection among donors who are repeat reactive on serology screening tests. Typically 80% or more of donors who test repeat reactive on serological screening assays are negative on supplemental or confirmatory testing. Although the test performance of blood donation assays (i.e. the sensitivity and specificity) is very good, the total number donations which are screened each year in the US leads to large numbers of donors who test false positive because the tests are not perfect and are optimized for sensitivity for blood safety purposes: A false positive result (which results in an interdicted donation) is more acceptable than a false negative (which would result in a potentially infectious donation being transfused). As an example, a test with a specificity of 99.9% when used to screen 12,000,000 donations per year will lead to 12,000 persons being classified as false positive. Donations from donors who test repeat reactive but are not confirmed by supplemental testing have been shown to represent random events which are not associated with particular donor characteristics (such as demographics). Studies of infected and uninfected blood donors have previously used this strategy to identify controls for case-case control studies and research has shown that donors with false positive results on an initial screening tests are not infected . Additionally, false positive donors are contacted by blood collection centers to review their test results and to reassure them that they do not have an infection. These donors therefore represent an appropriate sample of the non-infected blood donor population and are ideal as a control population for TTI-positive cases since operationally, they also need to be contacted and counseled by the blood centers. A random sample of these

individuals with false reactive test results will serve as a comparison "control" group to the confirmed positive "case" donors in TTIMS. When contacted in previous studies, enrollment rates for false positive donors are similar to those of cases (between 50 to 75%). The blood donations from individuals with false positive test results are destroyed for precautionary reasons. Because control donors may have risk factors discovered as part of the TTIMS program (as may any other donor), further operational concerns are avoided with respect to linkage to a transfused blood donation. Assessing compliance with disclosure of risk by both infected and uninfected donors is important. The inclusion of false positive donors (controls) in an earlier study "REDS-II Transfusion-transmitted retrovirus and hepatitis virus rates and risk factors: Improving the safety of the US blood supply through hemovigilance" (OMB control number 0925-0630) identified that donors with deferrable behaviors who are not infected are presenting to donate blood. In this way the controls provide important information on behavior disclosure in uninfected donors.

TTIMS Specific Objectives

The specific objectives of the TTIMS risk factor evaluation component are to:

- Evaluate risk factors among TTI seropositive blood donors and controls (as defined above) by inviting them to participate in the behavioral interview portion of the TTIMS program, as soon as possible after final confirmatory test results are available and the donor is counseled regarding their laboratory findings by blood center staff. Behavioral risk factors and motivations will be ascertained on the TTIMS risk factor interview.

- Produce high quality scientific data to inform further improvements to the standard blood donor DHQ. The TTIMS behavioral interview will request information about current behavioral risk factors and related characteristics for individuals who have donated blood and been identified as eligible study subjects (case or control).

The TTIMS behavioral risk interview instrument will inquire into:

  - Standard demographics

  - HIV pre- and post-exposure prophylaxis and anti-retroviral therapy – This is a new area of investigation among HIV seropositive blood donors based on observations from blood centers that use of these medications has been reported in the course of HIV infection counseling.)

  - Motivations and rationale for donating blood – (This information is key to understanding what motivates an at-risk individual to proceed with donation and not disclose deferrable risk behaviors. A particular focus of study will be to follow-up on the recent NCHS data showing that donor screening results are commonly based on a lack of attention (or lack of appropriate responses) to the content of screening questions based on internal perceptions of safety rather than a knowing misrepresentation of risk for personal gain.

- Specifics of sexual, drug, parenteral, and contact exposures – including questions to evaluate donor perceptions of monogamy. (The risks of acquiring hepatitis and HIV are well-known. What is not fully understood and will be addressed by TTIMS are the dynamics of individual perceptions and actions regarding the donation policy and process among at-risk donors, especially during a time of major policy change. For example, the December, 2015 changes in FDA policy regarding deferrals for possible MSM HIV risk modified a policy that had been in place for 32 years). These dynamics should be measurable by the outcome measures of TTIMS, for which the risk history questionnaire comprises a key component. An understanding of these dynamics is critical to providing FDA with the knowledge needed to oversee the predictive value of current and future donor behavioral screening. The ascertainment of detailed exposure histories will permit the FDA to model the impact of the change to a 1-year MSM deferral as well as modeling future modifications to current policies.

TTIMS will analyze integrated risk factor and TTI test data concurrently. When considered together these data may suggest that blood centers may not be achieving the same degree of success in donor screening and educational efforts to prevent donation by donors with risk behaviors across all risk subsets and demographic groups; and may engender the need for further evaluations of the DHQ or education materials.

Purpose and Use of the Information Collection

FDA intends to interview blood donors to collect risk factor information associated with testing positive for transfusion-transmissible infections (TTI). This collection of information is part of a larger initiative called TTIMS, which is a collaborative project funded by FDA, the NHLBI, and HHS/OASH with input from other agencies in HHS including the Centers for Disease Control and Prevention (CDC). FDA will use these scientific data collected through such interview-based risk factor elicitation of blood donors to monitor and help ensure the safety of the United States blood supply.

FDA issued a document entitled ‘‘Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products, Guidance for Industry’’ dated December 2015, which changed the blood donor criterion for MSM from an indefinite (permanent) deferral to a 12-month deferral since last MSM contact. The impact of this change in the deferral criteria requires a national monitoring effort as part of TTIMS to assess if the relative proportions of risk factors for infection in blood donors have changed following the adoption of the 12-month donor deferral for MSM. TTIMS will use similar procedures as the ones used in previous OMB approved information collection “Transfusion-transmitted retrovirus and hepatitis virus rates and risk factors: Improving the safety of the US blood supply through hemovigilance” (OMB control number 0925-0630) to monitor and evaluate risk factors among HIV-positive donors and recently HCV or HBV infected donors as well as controls. The overall TTIMS program will help identify the specific risk factors for TTI and their prevalence in blood donors, and help inform FDA on the proportion of incident (new) infections among all HIV positive blood donors. Donations with incident infections have the greatest

potential transmission risk because they could be missed during routine blood screening. TTIMS will help FDA evaluate the effectiveness of screening strategies in reducing the risk of HIV and hepatitis transmission from at-risk donors. This will be accomplished by evaluating unexpected consequences associated with the recent change in donor deferral policy such as a relative increase in HIV or hepatitis incidence among donors, or significant quantitative changes in the relative proportions or characteristics of the risk behaviors associated with donor TTI risks as determined by the TTIMS risk evaluation component of the program. These data also will inform FDA regarding future blood donor deferral policy options to reduce the risk of HIV transmission, including the feasibility of moving from the existing time-based deferrals to alternate approaches such as the use of individual risk assessments. Over time, TTIMS may also inform the design of potential studies to evaluate the feasibility and effectiveness of such alternative deferral options.

2. Use of Improved Information Technology and Burden Reduction

There are three possible routes of participant contact for the risk factor evaluation which are intended to minimize the burden of participation in the project by allowing donors to participate in the manner that is preferred by each donor.

- The primary route of participation in this project will be by telephone interviews of donors conducted for study data collection by trained donor counselors. Donor counselor-initiated phone contact will occur in which the donor counselors will follow-up to see if the donor received the notification letter and counseling materials mailed to donors using routine blood bank procedures. Donor counselors will attempt to contact donors up to three times by telephone, email, or text message. If the project staff are unable to reach a donor after three attempts the donor will be classified as lost to follow-up.

- Donor-initiated telephone contact following receipt of disease marker testing results and counseling materials sent to the donor via standard mail (HCV and HBV confirmed positive results and for all false positive results). Donors who are notified by mail whether confirmed or false positive are encouraged to call donor counselors to discuss the results and any additional questions the donors may have.

- In-person interviews may occur when a donor returns to the blood center for counseling (expected for HIV-positive donors) but donors who are positive for other viral markers could also seek in-person counseling. False positive donors may also seek in-person counseling.

The donor counselors will use an internet-based survey questionnaire program to automatically capture donor responses into a consolidated research database. Efforts to minimize respondent burden are described below:

- In-person or telephone interviews conducted using internet-based programs rather than self-administered questionnaire will help reduce respondent burden. Participants will be guided through all questions.

- Questionnaires include built-in skip patterns so that respondents are only asked relevant questions rather than all questions. Also, while the questions for both cases and controls are mostly identical, some questions will only be asked of donors with confirmed positive donations.

- The questionnaire contains risk behavior questions previously used in large-scale CDC surveys, and in the previous OMB approved project "REDS-II Transfusion-transmitted retrovirus and hepatitis virus rates and risk factors: Improving the safety of the US blood supply through hemovigilance" (OMB control number 0925-0630). The content is focused on common and less common routes of viral infection acquisition. The content does not include investigation of new or unproven routes of infection acquisition.

FDA is not aware of any other improved technology to reduce the burden.

3. Efforts to Identify Duplication and Use of Similar Information

No single comprehensive blood donor surveillance system exists in the United States to monitor TTI in blood donors.

Previous assessments of risk factor profiles among blood donors found to be positive for HIV were funded by CDC for approximately 10 years after implementation of HIV serologic screening of blood donors in the mid-1980s, whereas studies of HCV seropositive donors, funded by NIH, were conducted in the early 1990s. Information on current risk factors in blood donors as assessed using analytical study designs was next evaluated by the "REDS-II Transfusion-transmitted retrovirus and hepatitis virus rates and risk factors: Improving the safety of the US blood supply through hemovigilance" (OMB control number 0925-630). Through a risk factor questionnaire, this study elicited risk factors in blood donors who tested confirmed positive for one of four transfusion-transmissible infections: HIV, HCV, HBV, and Human T-cell Lymphotropic virus. The study also elicited risk factors from donors who did not have any infections (controls) and compared their responses to those of the donors with confirmed infection (cases). Results from the REDS–II study were published in 2015.

Until the completion of the REDS-II study, virtually no contemporary data on behavioral risk factors for the viral infections of interest in the TTIMS program were available. There are no duplicate sources of such information in the United States. While the CDC)conducted a series of donor risk evaluations in the 1990's, the current focus of CDC is on HIV prevention and treatment and current studies of blood donors are largely limited to participations in investigations of potential HIV transmissions that have occurred through blood products. Similarly, the NHLBI REDS-II program conducted highly successful epidemiologic studies of HIV in blood donors, however, this program was time-limited (incident HIV infections were not observed within the study). The

REDS-II program (by design) paved the way for the anticipated longer term TTIMS in numerous ways.

The collection of the proposed information is a vital part of the overall responsibility of the Federal Government and United States blood collection centers to ensure the safety of the national blood supply. FDA is responsible for protecting the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, biological products, medical devices, tobacco products, our nation's food supply, cosmetics and products that emit radiation. During its July 2, 2013 meeting, the DHHS Blood, Organ, and Tissue Senior Executive Council (BOTSEC), which includes representation by DHHS/OASH, CDC, NIH, Centers for Medicare and Medicaid Services (CMS), Health Resources Services Administration (HRSA), FDA, DHHS/Assistant Secretary for Planning and Evaluation (ASPE), DHHS/Assistant Secretary for Preparedness and Response (ASPR), and Agency for Healthcare Research and Quality (AHRQ), unanimously voted to enhance monitoring of TTIs in the United States by creating TTIMS.

Data collected in this project will be of practical use to the blood banking community and to the Federal Government (See specific aims of the study in Section A.1). In addition to peer-reviewed scientific publication, we anticipate data requests for presentations by Federal and non-Federal agencies, including the FDA Blood Products Advisory Committee, the DHHS Advisory Committee on Blood and Tissue Safety and Availability, the AABB Transfusion-Transmitted Diseases Committee, and the America's Blood Centers Association.

4. Impact on Small Businesses or Other Small Entities

No small businesses will be involved in this information collection.

5. Consequences of Collecting the Information Less Frequently

Study participants will be interviewed once only. Donors who agree to participate will be consented and asked to participate in the in-person or telephone interview. There is no follow-up involved. Less frequent collection of data would directly impair efforts to monitor trends in the infection risk factors reported by donors.

There are no technical or legal obstacles to reduce the burden.

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

There are no special circumstances for this collection of information.

7. 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 September 30, 2016 (80 FR 67358).

FDA received a few comments from the public. FDA concurs with one comment that providing more information to the blood center and FDA may aid in prevention of

transmission of infectious disease and is critical to the safety of the blood supply. Four comments received were not responsive to the comment request on the four specified aspects of the collection of information. None of the responses specifically commented on any of the proposed questions, nor did they request that the FDA make any other changes to the Donor Risk Assessment Questionnaire. Furthermore, the responses did not provide any data or explanation that would support a change regarding the information collection requirements.

8. Explanation of Any Payment or Gift to Respondents

Confirmed positive (case) and control donors will receive $75 for completing the interview. The participation incentive will be sent to each donor within six weeks following the completion of the interview. The incentives used for the study are justified on the basis of several considerations, as follows:

- First, the seropositive blood donors under study are a rare and hard-to-reach population. Approximately 1 out of every 40,000 donors has HIV. They represent a tiny fraction of the individuals who donate blood. Maximizing the participation of all donors with HIV infection and newly acquired HBV or HCV infection is particularly important to achieve a representative assessment of contemporary risk factors, i.e., the behaviors that likely led to acquisition of infection before donating blood. Many of the risk behaviors the project is inquiring about on the TTIMS risk factor interview should have been disclosed at the time of blood donation. If disclosed at that time, the disclosure would have made the donor ineligible for donation. TTIMS must overcome the barrier of previous non-disclosure of behavioral risks at the time of the proposed post-donation interview. This situation is different than general population surveys because donors with infection cannot be identified any other way than through donation. There are no other methods to identify these people for the risk factor interview.

- Second, the incentive contributes to improved disclosure by acknowledging the participants for frank reporting of sensitive and private behavior. As for cases, disclosure of risk behaviors in controls is equally important. In the " REDS-II Transfusion-transmitted retrovirus and hepatitis virus rates and risk factors: Improving the safety of the US blood supply through hemovigilance" high rates of undisclosed risk behaviors in uninfected false-positive (control) donors were found. For example, 1.7% of uninfected male controls in that study reported they had deferrable MSM behavior. This indicates the project must also overcome barriers to disclosure that are present in control donors.

- Third, the majority of interviews will be conducted by telephone at the time of first voice contact with the donors. It is very important to use this opportunity to enroll the potential participants in the project and we believe that offering incentives will help the donor counselors and physicians to gain consent for participation. From the experience in previous studies of infectious markers in

blood donors, it is best to complete interviews of risks factors during the first voice contact. Payment can help to facilitate the willingness to complete the risk factor questionnaire.

- Fourth, we will be seeking verbal consent to ask the study participants sensitive questions regarding private and personal behaviors. The payment is intended to recognize and thank each participant for taking the time to answer the questions as honestly as possible.

- Fifth, for the OMB-cleared REDS-II risk factor study (OMB control number 0925-630) cases were provided $75 reimbursement. Using the US BLS inflation calculator, (https://data.bls.gov/cgi-bin/cpicalc.pl?cost1=75.00&year1=201012&year2=201703), $75 in 2010 dollars is $83.43 today. As we will conduct the risk factor interviews for at least the next 3 years, we want to be certain to provide a reimbursement consistent with inflation-adjusted amounts and trends, and also reflecting the importance of each case and control interview. Importantly, for operational reasons the largest participating blood collection organization (ARC) is only able to offer reimbursement amounts in increments of $25.

- Sixth, a payment of $75 is consistent with other studies conducted with blood donors as illustrated by the following two examples:

  - An example of the reimbursement amount for donor-related studies is provided for a study of Dengue infection in donors from the ARC, see attached full consent, quoted from the informed consent for that study:

    "Will I be paid for participating?
    You will be compensated $100 for taking part in follow-up testing for dengue virus and completing the questionnaire. In the event that additional testing is requested for a second or multiple visits, if we find that you are likely truly infected with dengue virus, you would receive $150 for each of your additional visits."

    This Dengue study did include a return to the blood center to collect a blood sample and risk factor interview covering topics which are not nearly as sensitive as those planned for the TTIMS risk factor interview.

  - For donors who test positive and are requested to come back for additional sample collection, currently ARC offers $300. [Ultrio Plus Study of HIV, HCV, HBV, donor compensation is $300]. This does involve a return to the blood center to collect a blood sample, but does not include risk factor interviews.

Given the previous listed reason and examples of similar studies in blood banking, we believe $75 payment for cases and controls is an appropriate level for the TTIMS risk factor interviews.

9. Assurance of Confidentiality Provided to Respondents

The TTIMS risk evaluation project procedures are designed to protect the privacy of the participants. Each participating blood center has obtained human subjects approvals from relevant institutional review boards (IRBs) to conduct all aspects of the study. Each IRB has approved the privacy protection procedures we have included in the project. The only persons who will have access to personally identifying information (such as names, phone numbers, and addresses) are the donor counselors and clinicians within each blood collection organization. These personal identifiers are required to be used to properly identify each donor according to standard operational procedures at blood centers and to provide the reimbursement for participation. The information collected in the research databases will include unique project identification numbers. The data transferred to the researchers in this project will not include personally identifying information and from these data it will not be possible to trace back to personally identifying information. All study data will have a code numbers (donation identification number and donor number) instead of the participant's name. Participant names or the project code numbers will not be used in any summaries of the data, public presentations or published reports from this project.

In addition, a Certificate of Confidentiality specifically for the TTIMS project participants was obtained, thus preventing researchers from being legally compelled to release information reported by the participants. The Certificate of Confidentiality was obtained in accordance with Section 301(d) of the Public Health Service Act (Attachment 2). This Certificate prevents study staff from being compelled to disclose information that may identify participants by court order or other legal action. This protection lasts forever (even after death) for all project participants.

10. Justification for Sensitive Questions

The purpose of the interview questions is to collect donor demographic and behavioral profile data for comparing risk exposures between blood donors who test positive (cases) for HIV (NAT yield and seropositive), HCV (NAT yield), and/or HBV (NAT yield) to persons who test false positive i.e., are not infected (controls). This case-control study design will yield interview data on risk behaviors among blood donors that will be used to understand predominant risk behaviors associated with HIV, HBV, or HCV infections in United States blood donors. Routes and risks factors for infection acquisition are different for each of these three viral infections but may include male-to-male sex, having multiple heterosexual partners, injection drug use (IDU), exchanging money or drugs for sex, and some medical procedures. The only way to collect information on these risk factors is to directly ask participants to self-disclose these behaviors or exposures.

The results may also lead to the identification of areas of the standard donor health history questionnaire completed at the time of blood donation which would benefit from modification in ways that can decrease risk and improve risk behavior disclosure at the

time of donation, or by determining if aspects of the current pre-donation donor questionnaires are inadequate.

The project will inquire about potentially personally identifiable information (PII) as well as risk behaviors. Risk behaviors will be assessed in two or more time-based exposure periods, typically "ever" and "in the last year before the blood donation". Please see Attachment 3 for the study questionnaire and Attachment 4 for a question-by-question description and explanation. Donors will be asked to provide their date of birth, educational attainment, ethnicity and race. Of these data elements only date of birth is formally classified as PII by the National Institute of Standards and Technology. The information obtained will not be linked to any other data sources outside of TTIMS. Blood centers collect and must maintain PII, especially for donors who test positive for infections. The information collected will only include data that can be used to report results in broad groups as opposed to individuals. This information is necessary because it may identify that blood centers are not providing educational materials to specific groups of donors in ways that are most effective for donor eligibility assessment. The only way to assess and monitor trends between groups of blood donors is to collect a limited set of PII. Results will be reported in aggregate and never at the individual donor level. By allowing donors to indicate "other" or "mark all that apply" responses, the project provides routes for donors to choose how much PII they are willing to disclose. This information collection will not compel donors to provide any demographic information.

11. Estimates of Annualized Burden Hours and Costs

12 a. Annualized Hour Burden Estimate

The total annual estimated burden imposed by this collection of information is 450 hours annually.

Table 1.--Estimated Annual Reporting Burden

Type of Respondent	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Cases and Controls[1]	600	1	600	0.75 (45 minutes)	450

[1] Cases consist of virus-positive donations, and controls represent uninfected donors.

The estimated number of annual respondents is 600. The respondents will be persons who donated blood in the United States and these participants will be defined as cases and controls. The estimated number of respondents is based on an overall expected participation in the risk factor survey. It is estimated that each respondent will spend about 45 minutes (0.75 hours) during recruitment to participate and completing the telephone or in-person interview.

12b. Annualized Cost Burden Estimate

The estimated annualized cost to respondents $11,700.

Type of Respondent	Total Burden Hours	Hourly Wage Rate[1]	Total Respondent Costs
Cases and Controls	450	$26	$11,700

[1] average hourly earnings, all employees, private sector; the data is published by the Bureau of Labor Statistics and can be found on their Web site at http://www.bls.gov/webapps/legacy/cesbtab3.htm by checking the boxes marked "Average Hourly Earnings" and "Average Weekly Earnings", then clicking on the "Retrieve Data" button.

The respondent population of United States blood donors represents a wide variety and range of wage rates. The $25.53 per hour wage rate was selected based on Bureau of Labor Statistics reported overall labor force mean hourly earnings average hourly earnings for all employees in the private sector in April 2016. The $25.53 rate was rounded to $26 for this estimate.

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

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

13. Annualized Cost to the Federal Government

The annualized cost to the Federal Government for this information collection is $846,597. This is the cost of the Laboratory and Risk Factor Coordinating Center (LRCC) contract for the TTIMS project.

14. Explanation for Program Changes or Adjustments

This is a new data collection.

15. Plans for Tabulation and Publication and Project Time Schedule

The schedule for study activities is shown in table below.

Project Time Schedule	
Task	**Date of completion**
Risk Factor Survey Administration and Data Collection begins	1 week after OMB approval
Risk Factor Survey Administration and Data Collection ends	3 years after OMB approval –an extension of OMB approval will be sought
Data Compilation and QC	At monthly intervals after OMB approval
Data Analysis	10 – 14 months after OMB approval, and at 3 month intervals thereafter

Results will be disseminated to the scientific and blood banking community and others through peer-review journal publications. In addition, data requests for presentations by Federal and non-Federal agencies, including the FDA Blood Products Advisory Committee, the HHS Advisory Committee on Blood and Tissue Safety and Availability, the AABB Transfusion-Transmitted Diseases Committee, and the America's Blood Centers Association are expected.

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

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

17. Exceptions to Certification for Paperwork Reduction Act Submissions

    There are no exceptions to the certification.

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