Supporting Statement A for

Transfusion-transmitted retrovirus and hepatitis virus rates and risk factors: Improving the safety of the US blood supply through hemovigilance (NHLBI)

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SUPPORTING STATEMENT

A. Justification

A.1. Circumstances Making the Collection of Information Necessary

Information on current risk factors in blood donors as assessed using analytical study designs is largely unavailable in the US. This project represents a collaborative pilot research study that will include a comprehensive interview study of viral infection positive blood donors at the American Red Cross (ARC), Blood Systems Inc. (BSI) and New York Blood Center (NYBC) in order to identify the current predominant risk factors for virus positive donations and will also establish a donor biovigilance capacity that currently does not exist in the US. At this time it is not easy to integrate risk factor data and disease marker surveillance information within or across different blood collection organizations because common interview procedures and laboratory confirmation procedures are not being used and so we cannot easily tabulate and analyze behavioral risks or viral infections in US blood donors. This creates the potential for gaps in our understanding of absolute incidence and prevalence as well as risks that could lead to transfusion-transmitted disease. Combined data are critical for appropriate national surveillance efforts. For example, this information could be used to target educational interventions to reduce donations from persons with high risk behaviors. This is particularly important in the case of behaviors associated with incident (recently acquired) infections because these donations have the greatest potential transmission risk because they could be missed during routine testing. As part of the project a comprehensive research-quality biovigilance database will be created that integrates existing operational information on blood donors, disease marker testing and blood

components collected by participating organizations into a research database. The combined database will capture infectious disease and risk factor information on nearly 60% of all blood donors and donations in the country. Following successful completion of the risk factor interviews and research database development, the biovigilance network pilot can be expanded to include additional blood centers and/or re-focused on other safety threats as warranted, such as Xenotropic Murine Leukemia Virus-related Virus (XMRV). This pilot biovigilance network will thereby establish a standardized process for integration of information across blood collection organizations.

The **Specific Aims** are to:

1) Define consensus infectious disease testing classification algorithms for HIV, HCV, HBV, and HTLV that can be used to consistently classify donation testing results across blood collection organizations in the US. This will allow for better estimates of infection disease marker prevalence and incidence in the US.

2) Determine current behavioral risk factors associated with prevalent and incident (when possible) HIV, HCV, HBV and HTLV infections in blood donors, including parenteral and sexual risks, across the participating blood collection organizations using a case-control study design.

3) Determine infectious disease marker prevalence and incidence for HIV, HCV, HBV, and HTLV overall and by demographic characteristics in a large, geographically diverse sample of blood donors. This will be accomplished by forming research databases from operational data at BSI and NYBC into formats that can be combined with the ARC research database.

4) Analyze integrated risk factor and infectious marker testing data together because when taken together these may show that blood centers are not achieving the same degree of success in educational efforts to prevent donation by donors with risk behaviors across all demographic groups.

Collecting the proposed information is a vital part of the overall responsibility of the Federal Government and U.S. blood collection centers to ensure the safety and availability of the national blood supply. NHLBI has a Congressional mandate, Sec 421 [285b-3] and 422 [285b-4] to ensure the overall safety of the blood supply. An important aspect to this assurance is ongoing research regarding blood donation process and procedures to ensure the safety of donors while ensuring a blood supply adequate to fulfill the nation's need.

A.2. Purpose and use of information collection

Since 1989, the NHLBI-sponsored Retrovirus Epidemiology Donor Study (REDS) and REDS-II program has conducted epidemiologic, laboratory and survey research in the field of blood safety.

Data collected in this study 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 the traditional route of peer reviewed scientific publication, previous REDS-II study data were the subject of numerous requested presentations by Federal and non-Federal agencies, including the FDA Blood Products Advisory Committee, the HHS Advisory committee on Blood Safety and Availability, the AABB Transfusion-

Transmitted Diseases Committee, and the Americas Blood Centers Association. We anticipate similar requests for data generated from this study.

A.3. Use of Information Technology and Burden Reduction

In person and telephone interviews will be conducted for study data collection. There are three routes of study subject contact for this study:

1. In person interview when a donor returns to the blood center for counseling (expected for HIV positive) but donors positive for other viral markers could also seek in person counseling. False positive donors may also seek in-person counseling. Approximately 350 interviews will be conducted in-person and the remaining will all be via telephone.
2. Donor initiated telephone contact following receipt of disease marker testing results and counseling materials sent to the donor via standard mail (HCV, HBV, and HTLV results and for HIV 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.
3. Donor counselor initiated phone contact in which the donor counselors contact the donor to follow-up to see if the donor received the notification letter and counseling materials. Donor counselors will attempt to contact donors by telephone call up to 3 times by telephone. If we are unable to reach a donor after 3 attempts the donor will be classified as lost to follow-up.

Efforts to minimize respondent burden are described below:

- Planned in-person/telephone interviews rather than self-administered questionnaire will help reduce respondent burden.
- The questionnaire contains tried and tested questions from previous large scale CDC surveys.

A.4. Efforts to Identify Duplication and Use of Similar Information

Literature search shows that information on current risk factors in blood donors as assessed using analytical study designs is largely unavailable in the US. Studies of risk factor profiles among HIV-infected donors were funded by the CDC for approximately 10 years after implementation of serologic screening in the mid-1980s, whereas studies of HTLV- and HCV-seropositive (and indeterminate) donors, funded by NIH, were conducted in the early 1990s, but unfortunately, none of these studies is ongoing. This information is not routinely collected by U.S. blood collection centers in the course of their regular donor screening operations.

A.5. Impact on Small Businesses or Other Small Entities

Small businesses or entities are not involved. All respondents are individual blood donors.

A.6. Consequences of Collecting the Information Less Frequently

As mentioned in the earlier sections, study participants will be interviewed once only. Donors who agree to participate will be consented and asked to participate in the in-person or phone interview. There is no follow-up involved.

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

The proposed data collection is consistent with 5 CFR 1320.5.

A.8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside Agency

The 60-day Federal Register Notice was published on September 28, 2010, Volume75, No. 187, pages 59724-59725. Comments were received and a detailed response was submitted by the Project Officer on November 16, 2010 (see Attachment 6). There has been consultation outside of NHLBI to conceptualize and design the proposed study. The final study design was developed, reviewed, and approved by the REDS-II subcommittee, and the Observational Study Monitoring Board (OSMB) (see Attachment 2 for study protocol).

A.9. Explanation of Any Payment or Gifts to Respondents

Confirmed positive donors will receive $75 for completing the interview. The participation incentive will be sent to each donor or can be picked up at the respective donor clinics within two weeks following the completion of the interview. A $35 participation incentive will be provided to false positive (control) donors.

The incentives used for the study are justified on the basis of three considerations. First, the majority of interviews will be conducted by telephone at the time of first voice contact with the donors. It is very important that we seize upon this opportunity to enroll the potential participants in the study and we believe that offering incentives will help the donor counselors and physicians to gain consent for participation in the study. From our experience in previous studies of infectious markers in blood donors, it is best to

complete interviews of risks factors during the first voice contact. Incentives can help to facilitate the willingness to complete the risk factor questionnaire.

Second, we will be seeking verbal consent to ask the study participants sensitive questions regarding private and personal behaviors. The incentives are intended to recognize and thank each subject for taking the time to answer the questions as honestly as possible. Third, the two-tiered incentive schedule has been guided by the following factor. The risk factor questionnaire is designed with skip patterns consisting of initial screening questions that ask if the participant has a specific risk behavior or exposure. If the participant says yes, then additional questions are asked to get more specific details. It is expected that cases will have more risk factors and so it will take longer for cases to complete the questionnaire.

To more closely parallel other government funded interview studies we have decided to modify the incentive amounts. We will pay each case $75 incentive for a completed interview and will pay each control $35 for a completed interview. The two tiered incentive schedule remains in place because of the expected time difference to the complete the interview. .

The incentive for participation is structured so that the expected amount of time necessary to complete the risk factor questionnaire is commensurate with the incentive amount. While it appears that cases and controls will be answering nearly the same number of questions, the questionnaire is designed with skip patterns. With the expectation that cases will have more risk behaviors or exposures to report, it will take longer for cases on average to complete the questionnaire than it will for controls. The reimbursement schedule is designed to reflect this difference. Our goal is to reimburse

participants for total time it will take to complete the risk factor interview because complete answers for all questions on the questionnaire are critical for the success of the research project.

A.10. Assurance of Confidentiality Provided to Respondents

The study procedures are designed to protect the privacy of the study participants. Each participating blood centers has obtained human subjects approval from relevant IRBs to conduct all aspects of the study. Each IRB has approved the privacy procedures we have built into the study design. The only persons who will have access to personally identifying information are the donor counselors and physicians within in each blood collection organization. The personally identifying information will be used to properly identify each donor according to standard operation procedures and to provide the reimbursement for participation. The information collected in the research databases will include unique study identification numbers. The data transferred to the researchers in this project will not include personally identifying information and from this data it will not be possible to trace back to personally identifying information. All study data will have a code number instead of the participant's name. Participant's names or the study code numbers will not be used in any published reports about this study.

In addition, by specific addendum this study is covered by the Certificate of Confidentiality covering all of the Retrovirus Epidemiology Donor Study – II project thus preventing the researchers from being legally compelled to release information reported by the study participants. The Certificate of Confidentiality has been obtained in accordance with Section 301(d) of the Public Health Service Act (Attachment 5). This certificate prevents study staff from being able to disclose information that may identify

participants by court order or other legal action. This protection lasts forever (even after death) for all study participants.

Additionally, we have attached the memo from NIH Privacy Act Office stating that the Privacy Act is applicable to this collection. Please see Attachment 4 for this memo.

A.11. Justification for Sensitive Questions

The purpose of the interview questions is to collect donor profile data for comparing risk exposures between blood donors who test positive (cases) for HIV, HCV, HBV and/or HTLV to persons who test negative (controls). The responses will permit us to determine risk factors associated with each of the 4 viral infections among volunteer blood donors in the USA. A case control study will yield interview data on risk behaviors among blood donors that will be used; 1) to understand predominant risk behaviors associated with viral infections in blood in USA blood donors, for example: male-to-male sex, having multiple heterosexual partners, and injection drug use (IDU), 2) the results may also lead to suggestions for modification to current operational donor screening questionnaire in ways that can decrease risk and improve blood safety by determining if aspects of current donor questionnaire are inadequate. The questions for both cases and controls are identical, except questions 15 and 16 are only asked of confirmed positive donors. Through the results of routine laboratory testing of donated blood we will be able classify a donor as having recently acquired or longstanding infection. For this reason virtually potential risk behaviors are based on two or more exposure periods, ever or in the last year before the blood donation. Please see Attachment 3 for the study questionnaire and Attachment 4 for question by question description and explanation.

The questionnaire will be administered by trained donor counselors over the telephone or by medical doctors or trained donor counselors during an in-person interview at the time of notification.

Yes, we will be inquiring about PII information. We will ask donors to provide their date of birth, educational attainment, ethnicity and race. The information we obtain will not be linked to any data sources except for the blood donation records that establish whether a donor is confirmed positive or false positive for one of the viral infections of interest. Blood centers collect and must maintain personally identifying information, especially for donors who test positive for infections. The information we will collect will only include data that can be used to report results in broad groups as opposed to individuals. This information is necessary for us to collect because we 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 that we can assess whether this is the situation is to collect the PII information. Results will be reported in aggregate and never at the individual donor level. We believe that allowing donors to indicate “other” or “mark all that apply” provide routes for donors to choose how much information they are willing to disclose. We cannot compel donors to provide this information.

A.12. Estimates of Burden Hour Including Annualized Hourly Costs

The annualized cost to respondents is estimated at $43,326 based on $18 per hour. The respondent population of U.S. blood donors represents a wide variety and range of wage rates. Therefore, the $18.00 per hour wage rate was selected based on reported overall labor force mean hourly earnings in 2009. It is estimated that each

respondent will spend about 35 minutes (0.58 burden hours) reading and understanding the study information and completing a telephone or in-person interview.

Table A.12-1 ESTIMATES OF HOUR BURDEN

Type of Respondents	Number of Respondents	Frequency of Response	Average Time per response	Annual Hour Burden
Cases	1650	1	0.58	957
Controls	2500	1	0.58	1450
Total	4150			2407

Table A.12-2 ANNUALIZED COST TO RESPONDENTS

Type of Respondents	Number of Respondents	Frequency of Response	Average Time per respondents	Hourly Wage Rate	Respondent Cost
Cases	1650	1	0.58	$18	17,226
Controls	2500	1	0.58	$18	26,100
Total	4150				43,326

A.13. Estimates of Other Total Annual Cost Burden to Respondents or Record Keepers

There are no capital or start-up costs, and no maintenance or service cost components to report.

A.14. Annualized Cost to the Federal Government

The annualized cost to the Federal Government for the proposed study is estimated to be approximately $ 1,968,304 (per year).

A.15. Explanation for Program Changes or Adjustments

This submission constitutes a new collection of information.

A.16. Plans for Tabulation and Publication and Project Time Schedule

The schedule for study activities is shown in Table A.16.

A.16-1 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	10 month after OMB approval
Data compilation and QC	10 – 12 months after OMB approval
Data Analysis	10 – 14 months after OMB approval

Subject to NHLBI approval, data will be disseminated to the scientific and blood banking community and others through peer-review journal publications, and presentations at government (FDA Blood Products Advisory Committee) and professional meetings (AABB).

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

The OMB expiration date will be displayed in the upper-right hand corner of the questionnaire.

A.18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification for paperwork reduction act submissions.