Supporting Statement A for

The Prevalence and Incidence of HIV Molecular Variants and Their Correlation with Risk Behaviors and HIV Treatment in Brazilian Blood Donors (NHLBI)

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SUPPORTING STATEMENT

A. Justification

A.1. Circumstances Making the Collection of Information Necessary

Defining prevalence and incidence in blood donors and residual risk of HIV transmission by transfusions in Brazil may lead to new regulatory laws for introduction of new blood safety initiatives in Brazil. The data can be used to project the yield, safety impact and cost effectiveness of implementing enhanced testing strategies such as combination antigen-antibody assays and/or Nucleic Acid Testing (NAT). Determination of HIV risk factors in donors will support policy discussions over strategies to recruit the safest possible donors in Brazil, and will also yield significant information for HIV surveillance in Brazil when combined with prevalence and incidence data derived from general populations and high risk surveillance studies. The identification of incident HIV infections allows for clinical identification of recently transmitted strains of the virus in donor settings in the different cities of Brazil. This surveillance will monitor the trafficking of non-B subtypes and rates of transmission of drug resistant viral strains in low risk blood donors that can be compared with data from similar studies in high risk populations. Monitoring drug resistance strains is extremely important in a country that provides free antiretroviral (ARV) therapy for HIV infected individuals, many of whom have little education and modest resources, making compliance with drug regimens and hence resistance a serious problem. The findings from this project will also complement similar monitoring of HIV prevalence, incidence, transfusion risk and molecular variants in the US and other funded international REDS-II sites, thus allowing direct comparisons of these parameters on a global level.

Section 301 of the Public Health Service Act - 42 U.S.C. 241 authorizes the Secretary of Health and Human Services to conduct in the Public Health Service, and encourage, cooperate with, and render assistance to other appropriate public authorities, scientific institutions, and scientists in the conduct of, and promote the coordination of, research, investigations, experiments, demonstrations, and studies relating to the causes, diagnoses, treatment, control, and prevention of physical and mental diseases and impairments of man. This authority has been delegated to the NIH Director, and, in turn, further delegated to the IC Directors, subject to certain limitations which do not generally apply here.

22 U.S.C. 2101 and 22 U.S.C. 2102 authorize the Secretary, in carrying out his authority under any provision of law to conduct and support health research and research training, to make such use of health research and research training resources in participating foreign countries as he may deem necessary and desirable. This statutory provision may be read to authorize awards to foreign institutions under statutory provisions that authorize the Secretary to support health research and research training, such as 42 U.S.C. 241. This authority has been delegated to the NIH Director, and, in turn, further delegated to the IC Directors, subject to certain limitations which do not generally apply here.

A.2. Purpose and use of the information

Since 1989, the NHLBI-sponsored Retrovirus Epidemiology Donor Study (REDS) program has conducted epidemiologic, laboratory and survey research in the field of blood safety. In 2006, the REDS-II program initiated an international component, extending the scope of blood safety research to include investigators in Brazil and China. The goal of

the REDS-II International Component is to conduct epidemiologic, laboratory, and survey research on blood donors in selected resource-limited countries in regions seriously affected by the AIDS epidemic to help increase the safety and availability of blood for transfusion. Specific objectives for REDS-II International are to 1) assess and monitor the prevalence and incidence of HIV-1, HIV-2, and other existing as well as newly discovered infectious agents that pose a threat to blood safety, 2) assess risks of transfusion – transmitted infections, 3) assess the impact of existing and new blood donor screening methodologies on blood safety and availability, 4) evaluate characteristics and behaviors of blood donors including risk factors for acquiring HIV and other blood-borne agents, and 5) evaluate the donation process for ways to improve the safety and adequacy of the blood supply, and reduce infectious disease burden.

Data collected in this study will be of practical use to the blood banking community. In addition to the traditional route of peer reviewed scientific publication, previous REDS-I 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

A detailed HIV risk factor questionnaire will be administered to all subjects (See Attachment 1). The administration will be performed using a self-administered audio computer-assisted self-interview (ACASI) on a laptop computer in order to maximize reporting of stigmatized behaviors. A research assistant or nurse will provide the ACASI laptop (including earphones to be able to listen to the questions confidentially) to each subject at the blood center. The study subject will be shown how to use the computer to complete the interview by entering

basic demographic data with the help of the nurse, but will be given privacy to complete the rest of the questionnaire. The research assistant or nurse will remain available to answer questions and provide help as necessary. We chose ACASI to maximize reporting of stigmatized risk behaviors and to streamline the interview (built in skip patterns depending on initial responses so that donors are only prompted to answer questions about the details of a specific risk factor if they report having the risk). The ACASI format also uses electronic data capture which will reduce data entry errors. We anticipate that young Brazilian subjects will adapt easily to the computer interview, while older or illiterate donors will rely more heavily on the audio component and/or assistance from the research assistant. The questionnaire is based upon an instrument previously utilized and validated by the CDC in its HIV surveillance at U.S. blood banks with modifications appropriate to the Brazilian setting.

Donors will be assured of the confidentiality of their responses. Use of a Subject ID on the questionnaire will allow for tracking of survey responses without entering identifying information into the study database. The link between the Subject ID number and the identity of the donor is only maintained by the blood centers. This link is maintained so that HIV positive participants can be re-contacted with their genotyping and drug resistance test results or should the donor wish to withdraw from the study. The Coordinating Center (CC) will not have access to any donor identifying information.

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

This detailed risk factor information is not routinely collected by Brazilian blood collection centers in the course of their regular donor screening operations. Although several studies have been conducted in this area, there is no significant data related to the blood donor community. It is believed that the Blood Banks can play an important role in this effort due to HIV testing of large numbers of a young, otherwise healthy population. Regarding clinical

relevance of the proposed research, the Brazilian public health authorities have been responsive to the HIV epidemic, with prevention campaigns, provision of condoms, alternative testing sites, and most notably, the implementation of universal access to anti-retroviral treatment (ART).[1]

In 2004 Brazilian policies were changed to allow men who have sex with men (MSM) to donate blood if the last sexual intercourse occurred at least 12 months before the blood donation. The HIV prevalence in Brazil is 10 times higher than in the US and nucleic acid testing (NAT) has not been adopted to identify donors who recently acquired HIV infection. No data on HIV prevalence in blood donors has been published since this new policy was implemented.

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

Questionnaires will be administered only once to all subjects in an ACASI format on a laptop computer. This will help to study the demographics, history of previous donation and HIV testing, incentives and motivations for donating, sexual history, risks related to sexual partners, alcohol and drug use, medical history, other potential risk factors, work place exposures, and treatment. For this study the Brazilian Institute of Geography and Statistics (IBGE) basic ethnicity categories, white, black, yellow, brown and indigenous will be used. In addition to blood saved from their index blood donation, 30 ml of blood will be drawn at the time of the enrollment and interview.

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 requesting was published on May 29, 2008 and no comments were received. 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, the REDS-II Steering Committee, and the Observational Study Monitoring Board (OSMB) (See Attachment 3.1 for a complete list of members). The OSMB reviewed the final protocol and provided input and comments. Revisions were made to the Informed Consent document incorporating the suggestions of the OSMB to clearly state that strict confidentiality will be maintained throughout the study.

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

The project will pay R$ 12.00 (Brazilian currency) to reimburse participants for transportation expenses to and from the study center.

A.10. Assurance of Confidentiality Provided to Respondents

The Privacy Act does not apply to the proposed data collection since identifiable information will not be collected on this questionnaire.

A.11. Justification for Sensitive Questions

Special attention has been devoted to carefully design potentially sensitive questions in a straightforward and non-judgmental way. In Brazil there is no country-wide system, such as a deferred donor registry, to prevent a donor from attempting to donate at another blood center. A person at risk for HIV infection might donate blood at many blood banks and these questions will capture information on a donor donating at multiple locations. To assess a donor's level of altruism by determining if the donor exhibits altruistic behaviors in their daily life, we want to correlate their daily behavioral answers to assess how much of a factor altruism is when donating

blood. It is already known that donors will give a socially acceptable response rather than the real reason to donate when asked directly about blood donation. There is a major difference between asking a donor whether altruism is a motivation factor and measuring the degree to which donors report engaging in other altruistic behaviours. The survey instrument is comprised of questions designed to determine the donor's intention to get HIV testing through blood donation (test seeking). Blood bank serology testing may be attractive to people seeking HIV testing. We intend to ascertain donor's perceptions/confidence related to HIV serology performed by the blood bank as well as whether the blood screening serology testing was contributing factor in donating. Sexual lifestyle, including the number of sexual partners during the lifetime, increases the odds of having a sexually transmitted disease, as well as its spread. The sexual history responses will allow us to determine the most prevalent sexual patterns for the Brazilian blood donors and whether this pattern may or may not be correlated with specific serologic markers.

In many countries including Brazil, the path of HIV spread has moved from homosexual to heterosexual transmission. However this pattern has not been clearly demonstrated in blood donors. A better understanding of sexual risk factors for HIV may allow us to build more accurate questions to improve the donor qualification process. It may also help us to avoid potential discrimination and unnecessary loss of donors if the patterns of HIV transmission are not shown to be associated with sexual activity. The social matrix section is designed to capture detailed sexual information for up to 5 sexual partners in the 12 months before the last blood donation. The reasons for focusing on this period of time is that most blood borne disease and sexually transmitted disease can be diagnosed within 12 months of exposure; in Brazil having 6 or more sexual partners is the current number of partners leading to deferral for multiple sexual partners; in general, persons tend to maintain a standard pattern of sexual behavior in their lifetime (MSM, bisexual, heterosexual) as well as specific sexual practices that are relevant to identify higher risk behaviors for HIV transmission. We assume therefore that asking about more than 5 sexual partners will not provide any supplemental information. Responses from different partners will be

combined to determine the frequency that a donor has engaged in higher risk sexual behaviors. The individual responses are less important than the combined results across all partners that can be used to determine if specific sexual practices are associated with testing positive for HIV. We also intend to correlate the HIV incidence and prevalence among repeat and first time blood donors. These questions will guide future efforts to develop donor health history questions that will exclude donors with high risk.

The section on alcohol and drug use was included to evaluate the influence of social lifestyle in terms of alcohol and drug use. Use of mood altering substances may be associated with the risk of HIV acquisition. However this has not been clearly demonstrated in Brazilian blood donors. We also intend to evaluate whether specific serologic markers are related to riskier behaviors or illicit drug use.

The medical history section will capture exposures that could lead to HIV transmission. The section on other potential risk factors will obtain data related to rare risk factors for HIV infection. These questions are related to tattoos; acupuncture treatment; time spent in jail, prison, or a detention center; body piercings; and pedicure and manicure treatments at a salon or barber shop. Information from the section on work place exposures will be used only if a donor indicates they have no sexual, drug-related, or medical risks. However, donors who work in a health care profession or other social setting that could lead to exposure to blood or other body fluids could be at higher risk for HIV acquisition. Exposure and treatment questions will be used to ascertain if the blood donor knew of his/her HIV status at the time of blood donation, self-reported route and time of infection, and past or current antiretroviral therapy (ART). In Brazil, ART is universally available for HIV treatment. These questions will be useful for interpreting possible drug resistance patterns in the molecular surveillance component of the study. Please see Attachment 3.2 for a detailed justification for each question.

In addition, being aware of the possibly sensitive nature of the questions, the following steps will be taken to assure the confidentiality of respondents:

- The questionnaire is administered using audio computer-administered self interview (ACASI) program. The purpose of using a self-administered instrument is to ensure that potentially stigmatizing behaviors will be reported as honestly as possible without fear or concern that an interviewer would stand in judgment.
- All data will be stored in a secure location, accessible only to authorized study personnel.
- Donors are advised of the voluntary nature of their participation in the study and of the steps taken to ensure the confidentiality of the information collected. See Informed Consent Document, Attachment 2.

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

The annualized cost to respondents is estimated at $5,200 based on $6.50 per hour. It is estimated that each respondent will spend about 24 minutes (0.40 burden hours) including administration of the informed consent form and questionnaire completion instructions. The Brazilian minimum wage translates to approximately $1.50/hour. Through previous research, the Brazilian blood banks have learned that the majority of their blood donors work in jobs categorized by the Brazilian census as "Technical" positions. According to the census, these "Technical" workers make between $5 and $8/hour. For the purpose of this study, we have taken the mean of these salaries, $6.50/hour, to calculate an estimated cost of participation.

Table A.12-1: Estimated Total Annual Burden Hours

Estimated Number of Respondents	Estimated Number of Responses per Respondent	Average Burden Hours per Response	Estimated Total Annual Burden Hours Requested
2,000	1	0.40	800

Table A.12-2: Annualized Cost to Respondents

Estimated Number of Respondents	Estimated Total Annual Burden Hours Requested	Estimated Cost per Hour	Annualized cost to respondents
2,000	800	$6.50	$5200

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 $112,132 (per year).

A.15. Explanation for Program Changes or Adjustments

This questionnaire 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.

Table A.16: Study Timeline

Activity	Time Schedule
Initiate Study Recruitment Activities	November 2008
Participant Enrollment and Data Collection (2 years)	November 2008-October 2010
Data Management and Analysis	Ongoing through March 2011

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 (American Association of Blood Banks).

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 statement of OMB Form 83-I.

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[4] Busch MP, Glynn SA, Stramer SL, et al. A new strategy for estimating risks of transfusion-transmitted viral infections based on rates of detection of recently infected donors. Transfusion 2005;45(2):254-64.

[5] Tang JW, Pillay D. Transmission of HIV-1 drug resistance. J Clin Virol 2004;30(1):1-10..