SUPPORTING STATEMENT A

Does Pre-Donation Behavioral Deferral Increase the Safety of the Blood Supply?

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Introduction and Summary

In Brazilian blood collection centers, donor deferral is initiated either by the blood center staff, based on information disclosed by prospective donors, or by the donor through self-deferral. Either type of deferral occurs because of the belief that a donor's behavior, exposures, or history represents an increased risk to the safety of the blood supply.

Although the general eligibility criteria are mandated by the Brazilian Ministry of Health, the specific criteria for screening potential donors and the procedures for implementing them may vary across the regional blood collection centers. This study will focus on sexual behavior deferrals and their impact on blood safety. The two main study aims are: 1) To assess infectious disease marker prevalence in donors who are deferred for higher risk sexual and non-injection drug use behavior; and 2) To determine if the different deferral classification procedures used by different blood centers in Brazil lead to a measurable difference in disease marker prevalence in deferred donors. To do this, deferred donors who agree to participate in this study will be asked to complete an audio computer assisted self interview (ACASI) questionnaire that measures two content areas 1) motivations for attempting to donate, 2) additional information on the deferral and other potentially undisclosed deferrable behaviors. A blood sample will be collected from the deferred donors and tested for the panel of infections currently screened for in Brazil (HIV, Hepatitis C, Hepatitis B, Human T-lymphotropic virus, syphilis, and *Trypanosoma cruzi*) using the same high-throughput laboratory reagents and procedures that are used to screen donations. These deferred donor marker rates will be compared to

the marker rates among accepted donors with the same demographic characteristics. Marker rates in deferred donors will also be compared between the blood centers.

A. Justification

A.1. Circumstances Making the Collection of Information Necessary

While it is well-accepted that deferrals, as part of the "layers of safety" concept, increase the safety of the blood supply, studies with sufficiently large sample size to quantify HIV infection and other infectious marker rates in deferred donors are lacking. Evidence in support of increased safety is frequently inferred from studies conducted in other health care settings. For example, a small hospital-based case control study conducted in Brazil examined the association between infectious markers and body tattoos. Even though tattoos are not used as a criteria to determine blood donor eligibility in Brazil, having a tattoo was associated with HCV and also with having at least one positive infectious marker.(1) Significant associations were not independently observed for HIV, HBV, syphilis or Chagas. The authors reported an overall sensitivity of 11% and specificity of 97% for the presence of a tattoo as indicator of having HIV, HCV, HBV, or syphilis infection. The researchers then estimated the impact on blood donor selection and disease marker testing using the results from their hospital-based case control study. However, the assumptions such as disease marker prevalence of as much as 15% in donors who are deferred for tattoos and a prevalence of 4% of the potential donor base having a tattoo (2) do not represent current temporary deferrals in Brazil and do not address the most common behavior-related deferrals. A more detailed and targeted assessment of the value of relevant deferrals could be used to help inform blood donation policies in Brazil.

In the US, current HIV prevalence is so low that studies of HIV risk factor characteristics among deferred blood donors are impractical due to the large sample size required. The ten-fold higher HIV prevalence in Brazil [1,2] allows us to design a hypothesis-based study whose results will be directly applicable to Brazil, and more broadly may be relevant for other countries considering the utility of their donor deferral policies. Although technically recommended by the Brazilian Government, lack of funds and the poor cost-benefit ratio of HIV nucleic acid testing (NAT) have delayed its implementation in this upper-middle income country. Plans to implement NAT are currently being developed. Even if NAT were to be implemented, the residual risk of HIV infection would still be substantially higher than in USA. Additional studies that assess recruitment and deferral are therefore essential in further reducing the risk of transfusion-transmitted HIV infection. The Brazil Ministry of Health recommends a number of HIV risk factor questions in the standard blood donor questionnaire, but the effectiveness of these questions are unknown. Only preliminary studies of the HIV risk factor profiles have been conducted among Brazilian blood donors.

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 Institute Directors, subject to certain limitations which do not generally apply here.

22 U.S.C. 2101 and 22 U.S.C. 2102 (Attachment 1) 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 Institute 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.

Refer to the Introduction and Summary for information regarding the types of information that will be collected.

A.3. Use of Information Technology and Burden Reduction

An abbreviated version of a previously validated HIV risk factor questionnaire will be administered to all subjects (Attachment 2) to collect data regarding high risk behaviors. In order to maximize reporting of sensitive/personal behaviors and streamline data collection, the administration will be performed using a self-administered audio computer-assisted self-interview (ACASI) on a desk-top computer. The study subjects 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. Earphones will be provided to allow the donors to listen to the

questions in private. 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. As mentioned above, the questionnaire is an abbreviated version of the HIV Risk Factor Questionnaire used currently in the REDS-II Brazil study entitled "The Prevalence and Incidence of HIV Molecular Variants and Their Correlation With Risk Behaviors and HIV Treatment in Brazilian Blood Donors" (OMB CONTROL NUMBER: 0925-0597.) This longer questionnaire was 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. The new questionnaire has also been updated to include questions regarding the details of the current deferral and motivations to donate blood.

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

While the previous studies (1) have implied that deferred donors may have higher disease marker rates, to our knowledge there have been no Brazilian or studies in other countries focused on measuring actual disease marker rates in deferred donors that could then be used to estimate the positive predictive value of specific deferral categories. These deferred donors are not eligible to be enrolled in the HIV Risk Factor Study

(entitled “The Prevalence and Incidence of HIV Molecular Variants and Their Correlation With Risk Behaviors and HIV Treatment in Brazilian Blood Donors”), which uses a similar questionnaire, therefore they are not at risk for completing similar questionnaires multiple times. As much as possible, we will use demographic and other standard data already collected during the donation process, rather than re-collecting it during the course of the study.

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 at a Chosen Frequency

Questionnaires will be administered only once to all subjects in an ACASI format on a desktop computer. This will help to study the demographics, history of previous donation and HIV testing, and, sexual history. In addition, 24 ml of blood will be drawn at the time of the enrollment and interview to be tested for the panel of infections currently screened for in Brazil (HIV, HCV, HBV, HTLV, syphilis, and *Trypanosoma cruzi*).

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 February 24, 2010 in Volume 75, No. 36, pages 8367-8368. No comments were received. There has been consultation outside of NHLBI to conceptualize and design the proposed study. The final study design (Attachment 3) was developed, reviewed, and approved by the REDS-II subcommittee, the REDS-II Steering Committee (Attachment 4), and the Observational Study Monitoring Board (OSMB) (Attachment 5 for a complete list of members)..

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

No payment will be provided to the respondents.

A.10. Assurance of Confidentiality Provided to Respondents

This data collection is covered by NIH Privacy Act Systems of Record 09-25-0156, "Records of Participants in Programs and Respondents in Surveys Used to Evaluate Programs of the Public Health Service, HHS/PHS/NIH/OD." Please see Attachment 8 for the memo stating that Privacy Act is applicable to this protocol. 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. The Coordinating Center (CC) will not have access to any donor identifying information.

A.11. Justification for Sensitive Questions

Special attention has been devoted to carefully designing potentially sensitive questions in a straightforward and non-judgmental way. 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. For example, 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 motivation for attempting to donate and additional information on the deferral and other potentially undisclosed deferrable behaviors. Sexual lifestyle, including the number of sexual partners during the lifetime, increases the odds of having a sexually transmitted disease, as well its spread. The sexual history responses will allow us to determine the most prevalent sexual patterns for the Brazilian blood donors and whether certain behaviors may or may not be correlated with specific serologic markers. We plan to use response categories currently used by the Brazilian Institute of Geography and Statistics (IBGE) since these are the standard categories for reporting race in Brazil. These categories represent the broad population groups that reside in Brazil and will be familiar to the blood donors since this is what is used for their census. The OMB categories were developed to more accurately reflect the diverse U.S. population and not necessarily the population of other countries. Using the OMB standards may be confusing to the donor and may lead to mis-classification of the study population.

The general risk factor section will capture exposures that could lead to HIV and other infectious disease transmission. This section will obtain data related to tattoos;

acupuncture treatment; body piercings; and pedicure and manicure treatments at a salon or barber shop. 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 disease exposure. Exposure 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. Please see Attachment 6 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 7.

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

The annualized cost to respondents is estimated at $10,426 based on $6.50 per hour. It is estimated that each respondent will spend about 20 minutes (0.33 burden hours) including administration of the informed consent form and questionnaire completion instructions, and that 4,860 respondents will complete the questionnaire. 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: Estimates for hour burden and annualized cost to respondents

Estimated Number of Respondents	Estimated Number of Responses per Respondent	Average Burden Hours per Response	Estimated Total Annual Burden Hours Requested
4,860	1	0.33	1,604

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 total cost to the Federal Government for the proposed study is estimated to be approximately $224,264.

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 Activities

Activity	Time Schedule
Initiate Study Recruitment Activities	1 month after OMB approval
Participant Enrollment and Data Collection	2-24 months after OMB approval
Data Management and Analysis	25-36 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 (American Association of Blood Banks).

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

The OMB expiration date will be displayed on the first page of the ACASI questionnaire.

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

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

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