SUPPORTING STATEMENT B

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

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B. Collection of Information Employing Statistical Methods

B.1. Respondent Universe and Sampling Methods

During the proposed 6-month time period, it is expected that the four participating blood centers will see a total of approximately 250,000 individuals attempting to donate. The accepted ages for blood donation are 18-65 years but through previous data collected for the REDS-II Brazil Core Donation and Deferral Database, we are able to estimate that that approximately 85% will be less than 45years old, 60% will be male, and 30% will be first-time donors.

The expected sample size is 4,860 deferred donors. Roughly 75% of the sample will be first time donors who are deferred, and the other 25% will be repeat donors who are deferred. The disease marker rates among these two subgroups of deferred donors will be compared to the known disease marker rates of corresponding ‘accepted’ donors. An accepted donor is a donor who successfully completes a donation. Screening tests on these donations determines disease marker rates among donors.

Since first-time deferred donors constitute the majority of the sample and since the marker rates are presumed higher in first-time donors, a difference in marker prevalences between first-time deferred donors and first-time ‘accepted’ donors will be easier to detect.

Inclusion & Exclusion Criteria:

Subjects will be recruited for the study from those potential donors who are deferred during the health history assessment in categories of infectious disease exposures related to sexual and/or non-injection drug use.

Subjects will be excluded for the following reasons:

- **a.** Potential blood donors who refuse to participate
- **b.** Potential blood donors who are not Portuguese literate
- **c.** Potential donors who are deferred for reasons other than sexual or non-injection drug use behavior.

Subject Enrollment:.

Subjects will be enrolled for a six-month time period from approximately July 2010 – January 2011. If deferred donors do not participate in sufficient numbers to achieve study sample size requirements in a six-month study period, we will consider only including multiple sex partner deferrals in the study. This deferral is expected to be the most common and as a result the easiest to evaluate and also the potentially most important deferral that could be modified if there is no evidence of increased risk of infectious markers in donors who are deferred due to having multiple sexual partners. An evaluation of participation will be necessary within 2 months of study initiation to determine if actual enrollment rates match the projected rates. The two month evaluation will allow us to alter the deferral inclusion criteria if necessary.

Sample Size Calculations:

The expected sample size is 4860 deferred donors. Roughly 75% of the sample will be first time (FT) donors who are deferred, and the other 25% will be repeat

(RPT)donors who are deferred. The disease marker rates among these two subgroups of deferred donors will be compared to the known disease marker rates of corresponding 'accepted' donors. An accepted donor is a donor who successfully completes a donation. Screening tests on these donations determines disease marker rates among donors. These rates have been compiled in the 2008 REDS-II Brazil donation database and are shown in Table B.1A for the three markers of primary interest.

Since FT deferred donors constitute the majority of the sample and since the marker rates are presumed higher in FT donors, a difference in marker prevalence between FT deferred donors and FT 'accepted' donors will be easier to detect (as exhibited by the smaller Odds Ratios in Table B.1A). With the estimated sample size and 80% power we will be able to detect an odds ratio of 1.3 for the combined infectious marker prevalence in first time deferred donors compared to first time accepted donors when all deferred donors are combined together during analysis.

Aim 2 will compare the marker prevalence in the center that use non-specific deferral codes (i.e. Belo Horizonte) to marker prevalence in centers that use specific deferral codes (i.e. all other centers). Table B.1B shows the Odds Ratios (i.e. odds of positive marker in Belo Horizonte compared to odds of positive marker in other centers) that can be detected in the minimum expected sample size. Since the prevalence depend greatly on FT/RPT status of the deferred donor, the Odds Ratios will be tested stratified by FT/RPT status (hence the latter two columns of Table B.1B. are most relevant). With the estimated sample size and 80% power we will be able to detect an odds ratio of 1.6 for the combined infectious marker prevalence in first time deferred donors compared to

first time accepted donors when all deferred donors are combined together during analysis for the Belo Horizonte blood center.

Table B.1A:. Odds Ratios pertinent to Aim 1 that can be detected with 80% Power.

	Marker prevalence			Marker prevalence		
Infection	FT 'accepted' donors *	FT deferred donors	Odds Ratio	RPT 'accepted' donors *	RPT deferred donors	Odds Ratio
HIV	0.41%	0.74	1.8	0.19%	0.65%	3.4
HBV	0.26%	0.53%	2.0	0.02%	0.25%	12.5
syphilis	1.5%	2.1%	1.4	0.39%	1.03%	2.6
combined**	2.6%	3.4%	1.3	0.63%	1.31%	2.1

* Confirmatory marker prevalence of 'accepted' donors are derived from 2007-2008 REDS-II Brazil donation database.
** Combined prevalence of HBV, HCV, HIV, HTLV, and Syphilis

Table B.1B: Odds Ratios pertinent to Aim 2 that can be detected with 80% Power.

Infection		Overall		FT		RPT
HIV		2.3		2.5		4.4
HBV		2.7		2.9		7.5
syphilis		1.8		1.8		3.5
combined		1.6		1.6		3.1

B.2. Procedure for the Collection of Information

B.2.1. Questionnaire

A shortened HIV risk factor questionnaire will be administered to all subjects. 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.) A self-administered audio computer-assisted self-interview (ACASI) will be used in order to maximize reporting of stigmatized behaviors. 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. Earphones will be provided to allow the donor to listen to the questions in private. The research assistant or nurse will remain available to answer questions and provide help as necessary.

B.2.2 Phlebotomy for Clinical Testing

A phlebotomy of approximately 24 ml will be collected from the deferred donors and tested for the panel of infections currently screened for in Brazil (HIV, HCV, HBV, HTLV, syphilis, and *Trypanosoma cruzi*) using the same high-throughput laboratory reagents and procedures that are used to screen donations. Self-disclosed motivations and reasons for deferral will be reported. Comparison of deferred donor marker rates will be made to infectious marker testing of accepted donors with the same demographic characteristics captured in the available REDS-II Brazil donation database during the same time period of enrollment of the deferred donors in this study. Marker rates in deferred donors will also be compared between the blood centers that use detailed versus non-specific deferral codes.

B.2.3 Counseling and Medical Referrals

Deferred donors who test reactive for any infection will be informed of the results and counseled in accord with Brazilian and local regulations. Each of the participating

blood centers will conduct the notification and counseling procedures in the same manner as with their accepted blood donors who test reactive. First the donors are contacted by mail, informing them that one of the blood tests needs to be repeated and that they should return to the blood center for follow-up testing. Upon return to the blood center, the donors are counseled regarding their original test results as well as the false positive rates of the screening test in question. Then, they are asked to give another blood sample for confirmatory testing and notified of the result (either by mail if negative or phone if positive.) Those donors whose confirmatory results are positive are called back into the blood center for counseling by trained blood center staff, specializing in infectious disease issues, and provided the appropriate treatment referrals.

B.2.4 Data Analysis

B.2.4.1 Analysis of Infectious Disease Marker Rates

Disease marker rates (as a summary measure) and by each pathogen will be reported for the deferred donors. The prevalence of disease markers will be compared to those of demographically (age, gender, donor type and status) similar donors.
We will estimate the positive predictive value the behavioral deferrals using infectious marker test results as the relevant “gold standard”. The positive predictive value of a deferral is dependent on the prevalence of the deferral in the presenting donor population and the specificity of the tests used to detect each disease marker. Within deferral categories we will determine the disease marker positive test yield for all disease markers combined.

Multivariate modeling of the predictors of disease marker positive donors who are deferred among all donors who are deferred for higher risk behaviors will be conducted.

We expect to find a higher seroprevalence of HIV, HBV, and syphilis among donors with these deferrals when compared to demographically similar accepted blood donors. We do not expect that marker rates for HCV and HTLV will be higher because infection by sexual contact is less common for these viruses.

B.2.4.2 Analysis of Deferral Classification Procedures

Compare the prevalence of HIV, HBV, HCV, HTLV, and syphilis for donors who are deferred in a the center that uses non-specific deferral codes to the other blood centers that use specific deferral codes using t-test or other appropriate statistical tests.
The rate of infectious markers will be different (and likely lower) for the blood center that uses non-specific deferral codes than for the centers that use specific codes

B.3. Methods to Maximize Response Rates and Deal with Non-response

The study participants will be recruited during a six-month time period, during which time it is estimated that approximately 9,720 donors will be deferred due to the high risk behaviors of interest. We expect that approximately 50% of these deferred donors will agree to participate in the study (N=4860). See the table below for more details regarding the study sample.

	Sao Paulo	Belo Horizonte	Recife	Rio de Janeiro	Total
Donors Deferred for High Risk Behaviors (6 month period)	1782	4322	1560	2056	9720
Estimated Participation, 50%	891	2161	780	1028	4860

Every deferred donor who consents to participate in the study will be asked to complete the questionnaire. Since the questionnaire will be conducted in the user-friendly ACASI format, and also a research staff or a nurse will be available to provide assistance and answer questions, it is assumed that all donors participating in the study will respond to the questionnaire. They will be permitted to quit the ACASI questionnaire at anytime, with the partially completed data submitted to the Coordinating Center for analysis. The Coordinating Center will monitor the frequency of skipped items and report any patterns back to the study centers so that the research staff can address potential problems with the questionnaire or its administration.

B.4. Test of Procedures or Methods to be Undertaken

The pretesting of the ACASI questionnaire was conducted at Sao Paulo Blood Center by asking 9 donors to complete the questionnaire using a touch screen computer. Two of the donors had minimal (very low) education and they took approximately 40 minutes to complete the questions but had no problems using the ACASI tool. The average time spent to complete the questionnaire was 20 minutes and we have also used this for the calculation of burden hour. Also, the pretest provided valuable comments, leading to the refinement of questionnaire format and content.

B.5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

Attachment 5 lists the OSMB members. In addition we have consulted biostatisticians on statistical aspects of the study design; the blood centers researchers

responsible for enrollment, administering questionnaires, and collection of samples; and the CC staff for protocol development, study monitoring, and data management. Data analysis will be performed by the analytic staff at the CC that includes epidemiologists and biostatisticians, with assistance and oversight provided by the REDS International Steering Committee (see Attachment 4 for a complete list of Steering Committee members)