Supporting Statement B for

Investigating the Causes of Post Donation Information (PDI): Errors in the Donor Screening Process I/C

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TABLE OF CONTENTS

B. Collection of Information Employing Statistical Methods.....1

B.1. Respondent Universe and Sampling Methods.....1

B.2. Procedures for the Collection of Information.....4

B.3. Methods to Maximize Response Rates and Deal with Non-response.....10

B.4. Test of Procedures or Methods to be Undertaken.....11

B.5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data.....11

B. Collection of Information Employing Statistical Methods

B.1. Respondent Universe and Sampling Methods

B1a. Respondent Universe

The study sample will consist of three groups:

1. Donors with a PDI: all identified donors of interest with an FDA reportable donor suitability error classified as PDI at the REDS-II centers
2. Deferred donors: appropriately deferred (but not PDI deferred donors) at the REDS-II centers.
3. Accepted Donors: appropriately accepted for donation at the REDS-II centers

Only donors who are 18 years and older will be approached to participate in the study.

Table 1: Estimated number of donors needed for interviews

Donors	Travel	Medical	Blood/Disease Exposure (not drug related)	High Risk Behavior (Sex)	High Risk Behavior (Not Sex)	Total
PDI	12	12	12	12	12	60
Deferred	6	6	6	6	6	30
Accepted						12
Total	18	18	18	18	18	102

B1b. Sample Size Calculations:

As shown in Table 1, we plan to interview a total of 102 people, 60 of whom will be PDI donors, representing the primary group of interest in this study. We will include 12 PDI donors in each of the five broad categories of reasons of interest: travel-related; medical; blood/disease exposure - not drug related; high risk behavior - not involving sex; high risk behavior involving sex. Even though the interviews with the donors will be individual, we would like to form groups of similar PDI and deferred donors for analysis purposes. Table 2 lists the PDI/deferral reasons of interest within the 5 broad categories.

Table2: List of PDI/Deferral Reasons of Interest

Broad Categories	PDI/Deferral Reasons of Interest
Travel	Variant Creutzfeldt-Jakob Disease (vCJD)--Travel
	Travel to malaria area/history of malaria
Medical	History of surgery
	History of disease
	Received Proscar, Tegison or Accutane
	Received tissue allograft or transplanted organ
	Received medication, antibiotics, vaccine or immune globulin
	History of hepatitis (type not specified), HBV, HCV or jaundice
	Risk factors associated with CJD
	Donor received transfusion or clotting factors
Blood/Disease Exposure – not drug related	Accidental exposure to blood or body fluids
	Donor received body/ear piercing or tattoo or both
High Risk Behavior – Not sex	IV drug use
	Incarcerated/Multiple risks
	Non-sexual exposure to HIV, hepatitis (type not specified), HBV, HCV
High Risk Behavior - Sex	Male to male sex or female to male who had sex with male
	Exchanged sex for drugs or money/Sex with high risk behavior partner
	Had STD or Sex partner was positive for STD, HIV, HTLV, HBV, HCV, Hep
	Donor/sex partner lived in or immigrated from HIV group O area

Speaking with 12 PDI donors in each of these five categories will provide the opportunity to discover both similarities and differences across these groups in views of the health history-taking process. Although there is no "magic number," 12 persons in each of the five categories should provide a reasonable basis for finding any such variations. In addition, for analytic purposes, we will be able to combine responses for all 60 individuals and compare them to those for the appropriately deferred group (see below).

Our sampling plan calls for conducting interviews with a total of 30 donors who were appropriately deferred, 6 in each of the same five categories as above: travel-

related; medical; blood/disease exposure - not drug related; high risk behavior - not involving sex; high risk behavior involving sex. These individuals will serve as a kind of "natural" comparison group to the PDI donors, enabling us to consider whether and how they may differ from their PDI counterparts, for example, in views of the health-history taking process and/or awareness of the risk of deferral. While it will not be possible to draw generalizable conclusions based on these numbers, including this group as a point of comparison and potential contrast to the PDI donors will contribute to an enriched understanding of the issues involved in PDI. It is not planned to compare the two groups (PDI and deferred) statistically. The primary objective of the study is to gather detailed information on the errors and process leading to PDI, using the words and experiences of these potential donors/donors. The study investigators modified the analysis plan and aim to compare the experiences of the donors in these two categories and conduct a qualitative assessment. The study data will not be presented as frequencies or in any other quantitative manner. Therefore, interviewing equal number of donors in the two categories is not required.

Finally, we will interview a total of 12 accepted donors, who will be asked a more limited subset of the questions as compared with the PDI and deferred donors. These 12 individuals will provide a kind of "anchor," representing the third category of donors who figure into the donation process. Again, speaking with these individuals will give us an idea of whether and how they may be different than the PDI and deferred donors in their experiences with and attitudes toward the health history-taking process and other areas of interest.

B.2. Procedures for the Collection of Information

B2a. Responsibilities of Blood Center Research Staff – Recruitment of Subjects for Study

There are six participating blood centers located as indicated below:

- Blood center of Wisconsin, Milwaukee, WI;
- University of California-San Francisco and Blood Centers of the Pacific, San Francisco, CA;
- Emory University and American Red Cross-Southern Region, Atlanta, GA;
- Hoxworth Blood Center and the University of Cincinnati Medical Center, Cincinnati, OH;
- American Red Cross-New England Region, Dedham, MA and
- Institute for Transfusion Medicine and LifeSource Blood Services, Pittsburgh, PA.

The primary mission of all six blood centers is to collect blood to meet the demands within the U.S. for safe transfusion. Research is secondary. Each of these centers have agreed to participate in this protocol and their cooperation and participation is indicated by individual REDS-II research contracts with the NHLBI.

Telephone interviews will be conducted with enrolled donors to collect information regarding their knowledge, attitudes, behaviors and beliefs about the donor health history process. We plan to interview a total of 60 PDI donors, 30 properly deferred donors and 12 accepted donors. Overall, each centers' research staff will be responsible for recruiting 10 PDI, 5 deferred and 2 accepted donors. The coordinating center (Westat) has developed Manual of Standard Operating Procedures (MOP), that will provide information and step-wise directions for identifying, contacting, recruiting, mailing and consenting the potential donors. This MOP will also include general templates for telephone scripts, Invitation to participate brochure, and cover letter for the study packet. As required, these templates will then be modified and adapted by each participating center. Blood center staff will contact the identified donor and if the donor

agrees, will mail study packet to him/her. The study packet will include information material and the consent form for study participation and for the coordinating center to call and schedule an interview. The donor will be instructed to return the signed consent to the blood center. The interviewer from the coordinating center will then contact the donor to schedule an interview. We believe each center should project needing to contact approximately 68 donors. We are assuming that 50% of all approached donors will consent to participate in the study. Since the study aims to recruit donors in three different categories (PDI, deferred and accepted), it was decided to use 50% as an average response rate. For example, the response rate may be higher (above 75%) in the accepted and deferred donor categories and lower in the PDI category. Based on past experiences conducting semi-structured telephone interviews of this length and type, this is our best estimate across the three groups.

The number of donors approached at each center will provide margin for further attrition incase some of the consented donors change their mind and opt to discontinue when contacted by the coordinating center to schedule the interview. Because enrollment will be prospective, the overall number of donors to contact could potentially be less if consent rates are higher than expected. In other words, if the first PDI Malaria Travel deferral consents to contact and successfully completes the interview, the blood center would not need to recruit for this category again. They would, however, still need to recruit a vCJD donor from this category.

Within a week of their PDI identification, appropriate deferral or accepted donation, research staff will call the identified donor and obtain permission to mail a study packet and consent form. This packet will explain the study to the donor and will request him/her to return the signed consent form. By signing the consent form, the donor will agree to participate in this study and to be contacted by the coordinating center for scheduling an interview. Donors who do not respond to the letter within 7 business days will need to be called by the blood center research staff to confirm receipt of the letter and ascertain their willingness to participate in the study. In the letter and over the phone, donors will be asked to consent to having their contact information sent to the coordinating center so that the Westat interviewers can contact them to set up an

interview. If the donor subsequently refuses to participate when contacted by the coordinating center, this information will be relayed back to the blood center and the research staff will then have to find a replacement donor of the same type to interview. It should be stressed to the donors that the central coordinating center is conducting the study to ensure the anonymity of their responses and none of the individual donor responses will be sent back to the blood center. Detailed information on how to recruit for each type of donor is detailed in the following three sections.

B2b. Recruitment of Donors into the PDI sample

Each center will be responsible for recruiting 10 PDI donors for interviews. Data obtained from the six REDS-II centers indicate that the vast majority of PDI events are discovered at the time of a subsequent donation visit, usually because of new histories that result in a deferral. Less often, PDIs are discovered when donors contact the centers to inform them of changes in their health histories and through communication with donors during telerecruitment. For enrollment, the REDS-II centers' operations and/or quality assurance staff will notify the blood center research staff of any donor identified as having a PDI and a temporary or permanent deferral. This identification will occur on a real-time basis and potential PDI donors will be recruited prospectively to participate in the study. Centers will need to recruit several different types of PDI donors within each of the five groups to ensure a representative sample. For example, for the Travel category, it would be necessary to recruit both Malaria and vCJD PDI travel deferrals. Based on estimates from June 2006 – July 2007 for all 6 REDS-II centers, we anticipate that four months will provide sufficient time to allow for the identification and recruitment of donors for interviews. Table 3 details the total number of PDIs of interest in this study at the six REDS-II centers during June 2006 – July 2007. This table excludes donors who contact the center after donation to report a new diagnosis of a disease or an illness like a cold or flu that developed after their donation as this represents knowledge that was not known by the donor at the time of donation. We will not be pursuing PDI donors for the interviews that came to the attention of the center from hearsay or third-party sources.

Table 3: PDI Events at the 6 REDS-II centers from June 2006-July 2007

Interview Group	Representative PDIs Included	Number from July 1, 2006 – June 30, 2007
Travel	Creutzfeldt-Jakob Disease (vCJD) – travel; Travel to malaria endemic area/history of malaria	1209
Medical	History of any kind of hepatitis or jaundice; Donor received transfusion, clotting factors, tissue allograft, transplanted organ; History of disease or surgery; History of Cancer; Hx or risk factors associated with Creutzfeldt-Jakob Disease; Received finasteride, Tegison, Accutane, or Avodart; Received medication or antibiotics	418*
Blood/Disease Exposure	Donor received tattoo, ear or body piercing; Donor received accidental needle stick, exposed to blood or body fluids; Exposure to a disease	128
High Risk Behavior – Sexual	Sexually transmitted disease; Sex partner has or had a sexually transmitted disease; Sex partner tested reactive for HIV, HBV, HCV; Male to male sex; Female had sex with MSM; Sex with IV drug user; Donor or donor's sex partner lived in or immigrated from an HIV Group O risk area; Donor or donor's sex partner exchanged sex for drugs or money	206
High Risk Behavior – Non Sexual	IV drug use; Non-sexual exposure to HIV or any kind of hepatitis; Incarcerated	98

*Note – 174 of these were because of a history of cancer which is now not considered a PDI by the Food and Drug Administration.

B2c. Recruitment of Deferred Donors

Each center will be responsible for recruiting 5 deferred donors for interviews, one from each group of interest. Deferred donors will be recruited during the same period that the PDI donors are and in the same categories as the PDI donors. We suggest that when a PDI donor is identified, the research staff identify a deferral of the same type (as the PDI) from that week to try to recruit them into the study. Center research staff should double check that these deferred donors did not also have a PDI.

B2d. Recruitment of Accepted Donors

For comparison purposes, a smaller number of telephone interviews will be conducted with 12 accepted donors. Research staff at each center will need to recruit 2 accepted donors. However, since these donors have no particular risk factor to investigate, these interviews will only include the general portion of the interview and will have mostly closed ended questions.

B2e. Telephone Interviews Conducted by the Coordinating Center

After contact information is released to Westat, one of the interviewers with the study will try to make contact to conduct the interview or set up a time for the interview. All interviews will be conducted by telephone using senior level staff experienced in telephone interviews. Quality assurance procedures will also be applied to ensure consistency in the way that the questions are asked and establish that the interviewers are probing appropriately. In addition, throughout the course of the study, senior researchers will provide ongoing feedback to interviewers based on listening to selected recordings of their interviews. All interviews will be digitally-recorded and the recordings uploaded onto computers as dss files; these files will be transcribed and then coupled to the interviewer notes to form an analytic package for the data analysts.

Data Analysis

The data from the semi-structured interviews will be analyzed in two ways. The close-ended responses will be analyzed quantitatively and the open-ended responses will be analyzed as qualitative data.

Analysis of the qualitative data will take two possible paths, depending on how substantial these data prove to be. Included in this category are data gathered in three ways: 1) in other (specify) responses; 2) through interviewer probes for clarification of close-ended answers, and 3) in open-ended questions (of which there are relatively few in

the current version of the instrument). In many cases, particularly with the other/specify responses but also possibly with data obtained by probing or in open-ended questions, we may be able to back code the responses and then report their frequencies following the same analytic procedures as will be used for the quantitative data. To the extent that the probes help to clarify aspects of the respondents' interpretation of a question, it may make sense to report these clarifications in the context of the quantitative analysis.

In those cases where the data gathered through probing or in the open-ended questions have strong thematic content that helps to elucidate the key questions of interest and then we will apply full-fledged qualitative analytic procedures. Qualitative data analysis is a systematic process of finding meaningful recurrent themes and patterns. In this study, meaningfulness is defined with respect to central study questions of interest. So, as just one example, to the extent the data permit, we will be looking for systematic patterns in the reasons PDI donors give for not having initially reported the deferral event. We will also look for any meaningful variations in this regard across the five broad categories and by demographic factors such as age, gender, or blood donation center.

Once it is determined that the data warrant this level of analytic attention, the analysts will work from verbatim transcripts of the open-ended portions of the interviews as well as summary notes taken by the interviewer immediately following the interview. A common initial sample of transcripts will be read independently by at least two senior analysts, who will develop coding categories and then compare notes to reconcile any differences. The codes that emerge in this process are typically a combination of categories that derive from the structure of the instrument (e.g., perceptions of the health-

history taking process and "inductive" categories that derive from the specific content of the data. Sometimes the valence (positive or negative) of a statement also becomes part of the coding scheme.

Once a common coding scheme is established, relevant portions of each transcript containing the data to be coded will be read and coded according to that scheme by at least two different researchers participating in the study. Any further discrepancies of differences of interpretation that may arise will be reconciled through discussion and a consensus process.

After coding the data, the analysts will discuss the findings and create data displays, which may take the form of diagrams, matrices, tables, or "just plain text." [18] As a step in the process of qualitative data analysis, data display takes a step back from the coded data to reveal themes and patterns that might not be immediately apparent. For example, we might find that clusters of reasons for the PDI vary according to the nature of the PDI, and can show that in a concise, summarized format. The final step in the analytic process, taken only after multiple rounds of revisiting the data to ensure that the patterns are well-founded, will involve drawing conclusions from the summarized and displayed data. All analytic steps and assumptions that led up to the conclusions, including competing interpretations of the data, will be fully discussed in the final report.

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

We are assuming that 50% of all approached donors will consent to participate in the study. The number of donors approached at each center will provide margin for further attrition incase 50% of the consented donors change their mind and opt to discontinue when contacted by the coordinating center to schedule the interview.

Blood centers will approach 408 donors, assuming that 204 (50%) of these will consent to participate in the study and get contacted by the interviewer. We believe that out of these 204 blood donors, only 102 (50%) will actually participate in an interview.

No follow-up will be done with those blood donors who refuse to participate.

B.4. Test of Procedures

The cognitive testing of the discussion guide will be conducted at the Hoxworth Blood Center by interviewing a total of 6 donors. For this purpose, the blood center staff will identify 2 PDI and 2 deferred donors from the five broad categories of interest. They will also contact 2 accepted donors for study consent and interview. These donors will be approached and consented by following the same procedures that will be used for the actual study. After obtaining donor consent, telephone interviews will be conducted by trained interviewers at Westat. At the end of the interview, these donors will be queried about the questions asked during the interview and the interview process. Comments and feedback received will be used to refine the content and interview procedure that will be used for the actual study. These donors will also receive a compensation of $25.

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

Individuals consulted include 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 experts in qualitative data analysis along with epidemiologists and biostatisticians, with assistance and oversight provided by the REDS Steering Committee (see Attachment 5.5 for a complete list of Steering Committee members.)