

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

RISK FACTOR CASE CONTROL STUDY

Questions relating to survey objectives

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 to classify a donor as having recently acquired or longstanding infection. For this reason virtually all potential risk behaviors are based on two or more exposure periods, ever or in the last year before the blood donation.

The questionnaire is 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.

Front Page (Page 1)

This section is completed by the trained donor counselors or physicians before contacting the donors. Verbal consent will be obtained and basic study information is captured on this page. The donor counselor (or physician) will read the verbal consent information, answer any questions the potential study subject may have, and then the subject will either agree to or decline participation in the study.

SECTION A -INTERVIEW DATA

All portions of Section A will be completed by trained donor counselors or physicians before the interview begins. This information will be obtained from existing operational records at each blood center that were created when the donor consented to blood donation including infectious disease testing.

Study Number

Study Number will be used to identify each donor and is unique to this study and not linkable to any operational databases that could be used to identify an individual. This is the number that will be used to track all documents associated with participation in this study and during the analysis of data.

The following questionnaire items capture information on the administration of the questionnaire.

Date of interview

Interviewer initials

How contact with donor occurred

Interview language

Objective: The following questionnaire items are related to the specific tracking and record keeping information that are necessary to confirm and cross-check each donor's infectious disease testing results. This data is necessary to confirm case versus control status among other objectives such as determining where there are clusters of infections based on the zip code of residence.

Blood Unit Number

Blood Collection Center

Center Code

Donation Date

Donor Zip Code of Residence

Overall Testing Result

Infectious Disease Testing Results Table

SECTION B -DONOR DEMOGRAPHIC DATA

Section B and all remaining sections will be completed by the study subject. Each question will be asked by the trained counselors or physicians. All answers given by each subject will be recorded on the interview form by the person conducting the interview.

Factors known to be associated with HIV infection in the US general population include socio-economic status, age, race and gender. The data are critical in order to determine if risk factors in blood donors are similar to those reported for the general population of the country. In particular income appears to be very important and so the income questions are relatively detailed so that we may as accurately as possible determine household income brackets. The data recorded here will be used in multivariable modeling to control for potential confounding by these factors so that we may gain a more accurate understanding of the risk behaviors associated with each of the 4 viral infections.

Objective: To obtain demographic data for general risk stratification based on the background of the subjects.

Q1 What is your gender?

Q2 What is your birth date?

Q3 What is your country of birth?

Q4 What is the highest level of education you have completed?

Q5 Do you consider yourself Hispanic?

Q6 How would you describe your race?

Q7a What is your occupation?

Q7b Thinking about all family members in your household, what is your combined annual income, meaning the total pre-tax income from all sources earned in the past year?

Q7c Is your annual household income from all sources . . . (list of choices provided)?

Q7d At the end of the month, how much money are you able to save or put aside? Your best estimate is fine.

Q8 What is your current marital status?

Q9 If you are married or living with a partner, what is the gender of this person?

Objective: to obtain data related to whether a donor has donated blood before and if so the frequency of previous donation and motivations for donating blood. Motivations for donating are important so that we may identify the prevalence of persons seeking to have their blood tested for infectious markers.

Q10 Before your most recent donation had you previously donated blood at this or any other blood center or blood drive?

Q11a, 1-6 Please tell me whether any of the following reasons or factors contributed to your decision to donate blood. For each statement, please answer yes or no.

I wanted to donate blood to help someone in need

In response to a TV or radio campaign, or a phone call, or letter from the blood bank

I was encouraged or pressured by family, friends, coworkers, or by someone at a blood drive

I wanted to get my test results for my blood

I wanted to get the incentives for donating that the blood bank was offering

Q11b Is there another reason why you came to the blood center?

Q11c Can you please tell me the reason?

Q12, 1-5 Did any of the following factors influence your decision to come to the blood center? For each statement, please answer yes or no.

Blood center testing is confidential

Blood center testing is more accurate than at other test sites

Blood center testing is free

I think that the tests would identify any problem with my blood

None of these factors influenced my decision

Q13 I would like to ask your opinion about blood donation eligibility. For each of the following statements, please answer yes or no.

Do you think the current blood donor selection and screening policies are unfair?

Did your opinion about current blood donor selection and screening policies influence your decision to donate blood?

If you think that donor selection and screening policies are unfair, can you tell me what you think is unfair about them?

Q14 Is this the first time you have been told about testing repeat reactive or confirmed positive for _____?

The next two questions will only be asked of true positive cases:

Q15 How do you think you got infected with

Q16 Can you specify the date when you think you got infected?

Q17a At the time of donation were you aware that the activity you stated in question 15 could place you at a higher risk for infection?

Q17b How did you find out the activity you stated in question 15 could place you at higher risk for infection?

SECTION C -RISK FACTORS ASSESSMENT -Part I

Section C Part I and all remaining sections of the questionnaire will be completed by study subject in privacy. Each set of questions serves an important role because we are seeking to see if we can stratify the infected donor population based on the on the history of exposure and total number of exposures for known risk factors for infection.

Objective: to obtain data related to whether a donor has a single sexual partner in the last year. Increased number of partners is associated with increased risk of sexually transmitted infections.

Q18. In the last year "I have been monogamous," meaning I am in a committed relationship and have had sexual contact with only one partner.

Sexual History

Sexual lifestyle, including the number of sexual partners during the lifetime increases the odds of having a sexual transmitted disease, as well its spread. The sexual history will allow us to determine the most prevalent sexual patterns for USA blood donors and whether this pattern may or may not be correlated to specific serologic markers. The routes of sexually transmitted infections continue to be through both homosexual to heterosexual contact. However the current patterns for USA donors are not known. A better understanding of sexual risk factors for HIV and the other viral infections 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 specific sexual histories such as remote homosexual experiences. All questions will be asked of men and women, but with built in skip patterns a respondent will not be asked the entire list of questions if the person says they have not have any sexual contact with men and/or women.

Objective: To ascertain the respondents sexual history with male sexual partners. The time spans are relevant with respect to potential regulatory decision making by the US FDA. We are also asking about the frequency of use of condoms or protective barriers as this information is important for distinguishing between higher risk behaviors and behaviors with lower risk regardless of the number of sexual partners.

Q19a How many male sexual partners have you had in your lifetime? Please include both ongoing partners and one-time encounters with men.

Q19b In the last 5 years, how many male sexual partners have you had? Please include both ongoing partners and one-time encounters with men.

Q19c In the last 12 months, how many male sexual partners have you had? Please include both ongoing partners and one-time encounters with men.

Q19d Regarding your male sexual partners and one-time encounters with men in the last 12 months

(QUESTION 19c) , if you had vaginal or anal sex how often did you use condoms or protective barriers

Q19e Before your most recent blood donation, when was your last sexual contact with a male?

Objective: To ascertain the respondents sexual history with female sexual partners. The time spans are relevant with respect to potential regulatory decision making by the US FDA. We are also asking about the frequency of use of condoms or protective barriers as this information is important for distinguishing between higher risk behaviors and behaviors with lower risk regardless of the number of sexual partners.

Q20a How many female sexual partners have you had in your lifetime? Please include both ongoing partners and one-time encounters with women.

Q20b In the last 5 years, how many female sexual partners have you had? Please include both ongoing partners and one-time encounters with women.

Q20c In the last 12 months, how many female sexual partners have you had? Please include both ongoing partners and one-time encounters with women.

Q20d Regarding your female sexual partners and one-time encounters with women in the last 12 months (QUESTION 19c) , if you had vaginal or anal sex how often did you use condoms or protective barriers

Q20e Before your most recent blood donation, when was your last sexual contact with a female?

Objective: Previous history of sexually transmitted infections is a strong predictor of sexually transmitted viral infections in the general population. We will determine whether this is the case in the donor population based on the answers to the questions below. Recent history of sexually transmitted infections is expected to be more important than lifetime history.

Q21a Have you ever had a sexually transmitted disease, also known as a STD? Examples of STDs include gonorrhea, Chlamydia, syphilis, genital herpes, genital warts.

Q21b Can you tell me which STD(s)?

Q22a In the last 12 months, have you had a STD? Examples of STDs include gonorrhea, Chlamydia, syphilis, genital herpes, genital warts.

Q21b Can you tell me which STD(s)?

Drug Use

Objective: to obtain data related to whether a donor has used illegal drugs. Injection drug use is the most important risk factor related to drug use. However use of other “hard” drugs may also be an indicator of risk behaviors that could lead to infection acquisition. To ascertain the non-injected illegal drugs use and frequency.

Q23a Have you ever injected illegal drugs, steroids, or vitamins not prescribed by a doctor?

Q23b In the last 12 months, have you injected illegal drugs, steroids, or vitamins not prescribed by a doctor?

Q23c Can you please tell me what was injected?

Q24a Have you ever shared needles or syringes with another person?

Q24b In the last 12 months, have you shared needles or syringes with another person?

Q25a Have you ever used any illegal drugs that you did not inject, that is, drugs that are smoked, snorted, inhaled, or taken orally? Please do not include the use of marijuana when answering this question.

Q25b In the last 12 months, have you ever used any illegal drugs that you did not inject, that is, drugs that are smoked, snorted, inhaled, or taken orally? Please do not include the use of marijuana when answering this question.

SECTION C -RISK FACTORS ASSESSMENT -Part II

Objective: To obtain data related to rare risk factors for HIV, HBV, HCV or HTLV infection. Only if a donor indicates they have no sexual, drug-related, or medical risks would we presume that any of these exposures could be the route of infection acquisition. We need to determine if both cases and controls have similar exposure levels for these rare potential risk factors. Each of the exposures is known to be route of infection transmission for one or more of the 4 infections of interest.

- Q26a How many tattoos do you have on your body?
- Q26b In the last 12 months, have you had a new tattoo or had one re-applied?
- Q26c Where did you go to have your most recent tattoo(s) applied?
- Q27a In total, how many ear pies, have you had new ear piercings?
- Q28a In total, how many body piercings do you have?
- Q28b In the last 12 months, have you had new body piercings?
- Q29a Have you ever spent three or more nights in a row in any of the following
- Q29b In the last 12 months, have you spent three or more nights in a row in jail, prison, a detention center, a shelter, or group home?
- Q29c In total, how long have you spent in jail, prison, a detention center, a shelter, or a group home?

Sexual Partners Risks

The following section is related to known risks factors for blood borne disease in the donor's sexual partners in their lifetime. These questions will be useful for those cases where the respondents says they had 0 (zero) or no sexual partners in the 12 months before blood donation in Section C Part I of the questionnaire.

Objective: To determine the known risk factors for the donor's that are rare and to do determine potential risks the donor's sexual partners may have.

- Q30a Have you ever given or received money or drugs for sex
- Q30b In the last 12 months, have you given or received money or drugs for sex?
- Q31a Have you had sex with anyone who has injected illegal drugs, steroids or vitamins not prescribed by a doctor?
- Q31b In the last 12 months, have you had sex with anyone who has injected illegal drugs, steroids or vitamins not prescribed by a doctor?
- Q32a Have you ever had sex with a male who has also had sex with another male?
- Q33a Have you ever had sex with anyone who has tested positive for hepatitis?
- Q33b In the last 12 months, have you had sex with anyone who has tested positive for hepatitis?
- Q34a Have you ever had sex or intercourse with anyone who has tested positive for HIV?
- Q34b In the last 12 months, have you had sex or intercourse with anyone who has tested positive for HIV?
- Q35a Have you ever had sex or intercourse with anyone who has received a blood transfusion?
- Q35b In the last 12 months, have you had sex or intercourse with anyone who has received a blood transfusion?

Medical and Family History

Objective: To obtain data related to general medical history exposures, medical accidents and family history that could lead to transmission of 1 of the 4 viral infections of interest. Only if a donor

indicates they have no sexual or drug-related risks would we presume that medical exposure could be the route of infection acquisition.

- Q36a Have you ever received a blood transfusion?
- Q36b When was the last time you had a blood transfusion?
- Q37a Have you ever received a tissue or organ transplant?
- Q37b If yes, what type?
- Q38a Have you ever had an endoscopy (a medical test where a flexible tube is used to look inside of your throat and digestive system) or a colonoscopy (a medical test where a tube is used to look inside your colon/large intestine) ?
- Q38b In the last 12 months, have you had an endoscopy or a colonoscopy?
- Q38c When did you have your last endoscopy or colonoscopy?
- Q39a Have you ever received an intravenous or intramuscular injection such as for anesthesia or for other medical treatment (including for surgery, and diagnostic scans) in any location where health care is provided? For this question, please exclude any dental treatments, vaccinations, and acupuncture you may have had.
- Q39b In the last 12 months, have you received an intravenous or intramuscular injection such as for anesthesia or for other medical treatment (including for surgery, and diagnostic scans) in any location where health care is provided? For this question, please exclude any dental treatments, vaccinations, and acupuncture you may have had.
- Q40a Have you ever received injections for dental procedures?
- Q40b In the last 12 months, have you received injections for dental procedures?
- Q41a Have you ever received acupuncture?
- Q41b In the last 12 months, have you received acupuncture?
- Q42a Have you ever had a needle stick injury (accidentally been stuck by a needle or other sharp instrument after it was used for providing medical care to someone else) ?
- Q42b In the last 12 months, have you had a needle stick injury?
- Q43a Have you ever gotten someone else's blood, body fluids, vomit, or feces splashed into your eyes, mouth, or in an open skin wound?
- Q43b In the last 12 months, have you gotten someone else's blood, body fluids, vomit, or feces splashed into your eyes, mouth, or in an open skin wound?
- Q44a To the best of your knowledge, has anyone living in your household (including family or roommates) been infected with Hepatitis B virus or Hepatitis C virus?
- Q44b Can you tell me which person(s) is / are infected with Hepatitis B or C?
- Q45a Are any members of your family (meaning you, your parents, or your grandparents) from or have immigrated to the US from any of the following areas?
- Q45b Can you tell me which family member is from each area(s) you indicated?

Objective: To measure quality of life in donors. In addition the risk factor questionnaire includes questions on subjects' motivations for donating and a short assessment of the donor's quality of life at the time of the interview using the EuroQol Five Dimension (EQ-5D) instrument. The EQ-5D is a descriptive system of health-related quality of life consisting of five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) each of which can take one of three responses. The responses for each dimension are no problems/some or moderate problems/extreme problems, and the EQ-5D includes an open-ended overall quality of life assessment in which a standard vertical 20 cm visual analog scale (similar to a thermometer) is used for recording an individual's rating of his or her current health-related quality of life. Measures of quality of life infected donors and a comparison group have not been reported in the US.

Q46 Please indicate which statements best describe your own health state today.

Q46a Mobility

Q46b Self-care

Q46c Usual activities

Q46d Pain/Discomfort

Q46e Anxiety/Depression

Q47 To help people say how good or bad a health state is, I have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0. Can you picture the thermometer I am describing in your mind? (Pause for the person being interviewed to say yes, if the person says no, please re-read text). I would like you to indicate on a thermometer-like scale how good or bad your health is today, in your opinion. Please do this by telling me on a scale of 100 representing the best imaginable health state to 0 representing the worst imaginable health state, how good or bad your health state is today.

Objective: To obtain data related to a new potential threat to the blood supply – a new virus called XMRV. XMRV has been associated with Chronic Fatigue Syndrome, which is similar to but not the same as Fibromyalgia. These questions will tell how common these conditions are in infected and uninfected blood donors. The questions will be asked of all study subjects but are particularly important for control donors in order to assess the prevalence of these conditions in blood donors.

Q48 Have you ever been diagnosed with Chronic Fatigue Syndrome (sometimes called CFS or myalgic encephalopathy) as described here? Chronic Fatigue Syndrome is characterized by persistent or recurrent fatigue, diffuse muscle and bone pain, sleep disturbances, and subjective cognitive impairment of 6 months duration or longer. Symptoms are not caused by ongoing exertion; are not relieved by rest; and result in a substantial reduction of previous levels of occupational, educational, social, or personal activities.

Q49 Have you ever been diagnosed with fibromyalgia? Fibromyalgia is characterized by long-term, body-wide pain and tender points in joints, muscles, tendons, and other soft tissues, resulting in pain without weakness.

Detailed Question Justifications:

Please note that throughout the justification section, all questions that are indicated as *original* and *new* are based on questions used in previous infection disease risk factor studies in blood donors or for community-based studies. The content of these questions is largely similar to that of other studies. However the exact wording has been tailored for this specific study and mode of questionnaire administration. For these reasons we have classified each question as original and new. Only in the situation where we have used previously developed questions verbatim do we provide the source.

Study Number

Source: Original; new. The subject ID is a code number that identifies the blood donor as subject in the study. Through this code we will be able to examine; the blood donor's status for the following factors: type of donor (volunteer or replacement); frequency of blood donation (first time, repeated or lapsed); HIV testing results for the current donation.

*Blood Unit Number**Blood Collection Center**Center Code**Donation Date**Donor Zip Code of Residence**Overall Testing Result**Infectious Disease Testing Results Table*

The previous questions are not asked of the donor and are captured as part of standard operational procedures at all centers in the United States. The disease testing result table collects all relevant testing results into a single table. Overall testing result will define the case or control status for each study participant.

How contact with donor occurred

Source: Original; new. This will be used to track how study contact with the donor occurred.

Interview language

Source: Original; new. Donor's will be given the opportunity to consent and complete the questionnaire in English or Spanish as has been required by the Institutional Review Boards who have provided human subjects approval to complete the study.

Date of interview

Source: Original; new. This will be used to for study coordination and administration purposes.

Interviewer initials

Source: Original; new. This will be used to help identify potential problems during the interview or completion of the form so that we may contact each person who conducted each interview for clarification in the recording of responses.

- Q1 *Source: Original; new.* Self-reported gender. The risk of infection acquisition is different between males and females. We are allowing transgender as a response because gender is self-reported.
- Q2 *Source: Original; new.* Will be used with donation date to calculate exact age at the time of donation that tested true or false positive. Also necessary to ensure that only persons over the age of 18 participate in the study.
- Q3 *Source: Original; new.* The risk of 4 viral infections of interest can vary according to country of birth. This question is particularly important for HBV and HTLV infections.
- Q4 *Source: Original; new.* Lower education has been associated with increased risk of each of these infections. This information is necessary as educational attainment is a potential confounder of association between behavioral risk factors and each of the 4 viral infections.
- Q5 & Q6 *Source: Original; new.* Ethnicity and race are potential confounders of association between behavioral risk factors and each of the 4 viral infections.
- Q7a *Source: Original; new.* Certain occupations such as health care providers or persons who work in care facilities are at higher risk of HBV infection in particular, but could also be at higher risk for the other 3 viral infections in this study.
- Q7b, c, and d *Source: Original; new.* This information is necessary because income (socio-economic status) has recently been shown the most important predictor of HIV risk. Income is also a potential confounder of association between behavioral risk factors and each of the 4 viral infections.
- Q8 *Source: Original; new.* Marital status is also a potential confounder of association between behavioral risk factors and each of the 4 viral infections.
- Q9 *Source: Original; new.* The gender of a person's spouse will allow us to broadly classify the persons into groups without directly inquiring about sexual orientation.
- Q10 *Source: Original; new.* A donor's self-reported history of previous donation is important to ascertain so that we may determine if a donor with a long-standing (prevalent) may have posed a previous risk to blood recipients.
- Q11a, parts 1-5, b and c *Source: Original; new.* Each of the six queries is intended to inquire about the underlying reasons why each study participant tried to donate. It is important to assess whether any of these factors are associated with true positive donors so that we can potentially implement strategies to reduce donation by motivating factors that could place blood recipients at risk. 11b allows for the donor to indicate another reason and 11c asks the donor to tell us the other reason.
- Q12, parts 1-5 *Source: Original; new.* Each of the five queries is intended to inquire about whether specific aspects of blood donation testing contributed to the study subject's decision to donate blood. Because blood centers offer free, accurate and confidential testing it is possible that blood donors who have risk may use blood centers as locations for testing. It is important to assess whether any of these factors are associated with true positive donors so that we can potentially implement strategies to reduce donation by motivating factors that could place blood recipients at risk.

- Q13, parts 1-3 *Source: Original; new.* Blood centers have increasing concerns that some blood donors may be intentionally lying during the eligibility assessment process because they believe current regulations and rules are unfair. However, no data is currently available on this topic and so these questions will at least allow for donors to indicate if they perceive current rules to be unfair and if so what they think is unfair about the rules.
- Q14 *Source: Original; new.* We expect that most confirmed positive donors will not be aware of having an infection. However, we would like to determine how frequently donors with already known infections are specifically obtaining additional testing. This question will indicate if a donor knowingly donated a potentially infectious unit of blood. We also want to check to determine if the notification process is working as it is supposed to, so we will ask all study subjects this question regardless of case or control status.

The next two questions will only be asked of true positive cases only:

- Q15 *Source: Original; new.* This question is extremely sensitive but very important because most donors know what risk behavior may have lead to infection. We would like to know the response that each donor has about route of infection. Regardless of the answer provided we will continue with the interview.
- Q16 *Source: Original; new.* This question will help us to know if the risk behavior is recent or remote. The more recent the risk exposure the greater the chance that available testing could have (but didn't for all study subjects) missed the infection. If certain behaviors are reported to have occurred recently this tell blood centers that they need to be especially vigilant when inquiring about these particular risk behaviors.
- Q17a *Source: Original; new.* This question is intended to assess whether study subjects understand that risk behaviors they have may have disclosed are routes of infection acquisition. This question tests how well pre-donation information is performing in educating donors and also indicates whether donors are at least aware of general public health educational efforts regarding infectious disease risk reduction.
- Q17b *Source: Original; new.* This question will tell us whether blood center educational pamphlets or other educational efforts outside of the blood donation setting are where donors learned about infection risks.
- Q18 *Source: Original; new.* This question is important to understand potential policy changes for donor eligibility are most concerned about sexual exposures. Persons who answer yes to this question would not be expected to risk profiles that would place them in higher risk sexual exposure groups. The answer to this question will be compared for cases with each infection and controls to see if monogamy or not in the last year is associated with increased risk of infection.
- Q19a *Source: Original; new.* This question is designed to assess the estimated number of life-time male partners for each donor, regardless of sexual orientation. A high number of partners could be a marker for a person being at higher risk for HIV or HBV infection.
- Q19b *Source: Original; new.* This question is designed to assess the estimated number of male partners in the five years preceding the most recent blood donation for each donor, regardless sexual orientation. The five year interval is important for potential changes to donor eligibility regulations. A high number of partners could be a marker for a person being at higher risk for

HIV or HBV infection.

- Q19c *Source: Original; new.* This question is designed to assess the estimated number male partners in the year before donation for each donor, regardless sexual orientation. A high number of partners in the previous year could be a marker for a person being at higher risk for recently acquired HIV or HBV infection.
- Q19d *Source: Original; new.* This question will distinguish between persons who practice safer sex and those who do not. It is expected that persons who practice safer sex will be at lower risk for HIV, HBV, or HTLV infection. (HCV is generally not thought to be transmitted sexually.)
- Q19e *Source: Original; new.* The question will help to assess how recently the last sexual exposure was for each person regardless of gender or sexual orientation. Once again, very recent exposure poses the greatest risk of not being identified by blood testing and so it is important to know time period between donation and last sexual activity. This question is particularly important for confirmed positive donors, but will be asked of all study subjects so that comparisons can be made.
- Q20a *Source: Original; new.* This question is designed to assess the estimated number of life-time female partners for each donor, regardless of sexual orientation. A high number of partners could be a marker for a person being at higher risk for HIV or HBV infection.
- Q20b *Source: Original; new.* This question is designed to assess the estimated number of female partners in the five years preceding the most recent blood donation for each donor, regardless sexual orientation. The five year interval is important for potential changes to donor eligibility regulations. A high number of partners could be a marker for a person being at higher risk for HIV or HBV infection.
- Q20c *Source: Original; new.* This question is designed to assess the estimated number female partners in the year before donation for each donor, regardless sexual orientation. A high number of partners in the previous year could be a marker for a person being at higher risk for recently acquired HIV or HBV infection.
- Q20d *Source: Original; new.* This question will distinguish between persons who practice safer sex and those who do not. It is expected that persons who practice safer sex will be at lower risk for HIV, HBV, or HTLV infection. (HCV is generally not thought to be transmitted sexually.)
- Q20e *Source: Original; new.* The question will help to assess how recently the last sexual exposure was for each person regardless of gender or sexual orientation. Once again, very recent exposure poses the greatest risk of not being identified by blood testing and so it is important to know time period between donation and last sexual activity. This question is particularly important for confirmed positive donors, but will be asked of all study subjects so that comparisons can be made.
- Q21a *Source: Original; new.* Other common STDs are markers for the risk of sexual transmitted viral infections of interest in this study.
- Q21b *Source: Original; new.* We are asking for study subjects to report this information because we would like to see if a specific other STD is associated with risk of HIV or HBV.

- Q22a *Source: Original; new.* Recently acquired infections pose the greatest threat to the safety of the blood supply and study subjects who report recently acquired infection will have likely had recent sexual exposure even if they have not disclosed such exposure in questions 19 or 20.
- Q21b *Source: Original; new.* We are asking for study subjects to report this information because we would like to see if a specific other recently acquired STD is associated with risk of HIV or HBV.
- Q23a *Source: Original; new.* Non-prescribed and illegal injection drug use are high risk behaviors associated with the risk of HIV, HCV, HTLV, and to a lesser extent HBV acquisition. Comparing the rates of injection drug use between cases and controls is important for this study.
- Q23b *Source: Original; new.* Non-prescribed and illegal injection drug use are high risk behaviors associated with the risk of HIV, HCV, HTLV, and to a lesser extent HBV acquisition. Comparing the rates of recent injection drug use between cases and controls is important for this study.
- Q23c *Source: Original; new.* The previous parts of question 23 are compound questions. It is important to determine what substance(s) were injected in order to assess if particular injected drugs or vitamins are associated with the risk of acquisition of each of the 4 viral infections.
- Q24a *Source: Original; new.* Needle sharing is an exquisitely high risk behavior and we need to how prevalent it is in infected blood donors.
- Q24b *Source: Original; new.* Recent needle sharing is an exquisitely high risk behavior and we need to how prevalent it is in infected blood donors.
- Q25a *Source: Original; new.* Use of other “hard” illegal drugs is marker of risk behaviors.
- Q25b *Source: Original; new.* Use of other “hard” illegal drugs is marker of risk behaviors and recent use is more likely to be associated with confirmed positive infection.
- Q26a *Source: Original; new.* Historically tattoos and related body modification procedures have been risk factors for HBV and HCV infection and could also be risk factors for HIV and HTLV. The number of tattoos on a study subject’s body may be associated with infection.
- Q26b *Source: Original; new.* New tattoos may be associated with newly acquired infection.
- Q26c *Source: Original; new.* The location that a tattoo was applied is important because the equipment used in a licensed facility is far less likely to be the source of infection acquisition.
- Q27a *Source: Original; new.* Ear piercing could be an uncommon risk factors for HBV and HCV infection and could also be risk factors for HIV and HTLV. The number of tattoos on a study subject’s body may be associated with infection.
- Q28a *Source: Original; new.* Body piercing could be a risk factors for HBV and HCV infection and could also be risk factors for HIV and HTLV. The number of tattoos on a study subject’s body may be associated with infection.
- Q28b *Source: Original; new.* New body piercings may be associated with newly acquired infection.

- Q29a *Source: Original; new.* Incarceration or living in group facility are potential markers of undisclosed or unknown routes of exposure to HIV, HCV, and HBV.
- Q29b *Source: Original; new.* Recent incarceration or living in group facility may be associated with newly acquired infection.
- Q29c *Source: Original; new.* Longer duration of time incarcerated or in a group facility may represent higher risk of infection acquisition.
- Q30a *Source: Original; new.* This question will determine if the study subject has participated in the sex trade industry without specifically asking whether the person was a prostitute or “john”. Participation in the sex trade industry is a risk factor for sexually transmitted infections.
- Q30b *Source: Original; new.* This question will determine if the study subject has participated in the sex trade industry without specifically asking whether the person was a prostitute or “john”. Recent participation in the sex trade industry is a risk factor for recently acquired sexually transmitted infections.
- Q31a *Source: Original; new.* This question is designed to ascertain the blood donor’s risk based on having sex with an IDU partner at any time in his or her life. We will correlate this response to HIV infection status based on the results of the HIV testing of the blood donation. For example, a “yes” answer to this question could be route of infection acquisition for a donor who tests HIV positive
- Q31b *Source: Original; new.* This question is designed to ascertain the blood donor’s risk based on having sex with an IDU in the year before donating, which will reflect a relatively recent risk.
- Q32a *Source: Original; new.* This question is designed to rule-in or rule-out HIV acquisition via sexual contacts with homosexual or bisexual men.
- Q33a *Source: Original; new.* This question is designed to ascertain the blood donor’s risk based on having sex with an HCV or HBV positive partner at any time in his or her life.
- Q33b *Source: Original; new.* This question is designed to ascertain the blood donor’s risk based on having sex with an HCV or HBV positive partner in the year before donating, which will reflect a relatively recent risk.
- Q34a *Source: Original; new.* This question is designed to ascertain the blood donor’s risk based on having sex with an HIV positive partner at any time in his or her life.
- Q34b *Source: Original; new.* This question is designed to ascertain the blood donor’s risk based on having sex with an HIV positive partner in the year before donating, which will reflect a relatively recent risk.
- Q35a *Source: Original; new.* This question is designed to ascertain whether having sex with transfused person could be the route of acquisition for HIV or HBV.
- Q35b *Source: Original; new.* This question is designed to ascertain whether recent sexual contact with transfused person could be the route of recent acquisition for HIV or HBV.
- Q36a *Source: Original; new.* This question assesses history of previous transfusion in order to rule-in

or rule-out this potential route of infection acquisition. Have you ever received a blood transfusion?

- Q36b *Source: Original; new.* This question will provide further information on whether a history of blood transfusion could be the source of infection because the combination of disease marker testing will allow us to determine whether a donor has a recently acquired or long standing infection. If the study subject has remote previous transfusion but recent infection for HIV, HBV, or HCV the transfusion would not be the source of the infection.
- Q37a *Source: Original; new.* This question assesses history of organ transplantation in order to rule-in or rule-out this potential route of infection acquisition.
- Q37b *Source: Original; new.* The type of organ may be associated with certain infections for example HCV or HBV would be much more likely to result from liver transplantation.
- Q38a *Source: Original; new.* There have been clusters of HCV and HBV transmission due to improperly sterilized or improper re-use of medical equipment during colonoscopy/endoscopy. If a study subject indicates he or she has no other risk factors this could be the route of infection acquisition for any of the 4 viruses of interest and in particular the hepatitis viruses.
- Q38b *Source: Original; new.* This question will provide further information on whether a history of colonoscopy/endoscopy could be the source of infection because the combination of disease marker testing will allow us to determine whether a donor has a recently acquired or long standing infection. If the study subject has remote colonoscopy/endoscopy but recent infection, colonoscopy/endoscopy would not be the source of the infection.
- Q38c *Source: Original; new.* This question will provide specific information on the relationship between the timing of blood donation and recent colonoscopy/endoscopy. The timing is important for in suggesting this as a route of infection acquisition. In addition because we will ask this question of all study subjects we will have a much better understanding of the frequency of this type of exposure in blood donors.
- Q39a *Source: Original; new.* Injections are an important potential route of infection even if they occur in a medical setting. This question will help us to identify whether deep injections are associated with confirmed positive infections.
- Q39b *Source: Original; new.* Injections are an important potential route of infection even if they occur in a medical setting. This question will help us to identify whether recent deep injections are associated with confirmed positive infections.
- Q40a *Source: Original; new.* Dental injections have been the source of infections, but rarely. We would like to rule-out this as a likely route of infection.
- Q40b *Source: Original; new.* Dental injections have been the source of infections, but rarely. We would like to rule-out this as a likely route of recent infection.
- Q41a *Source: Original; new.* Acupuncture is thought to be a very rare route of infection acquisition. We would like to rule-out this as a likely route of infection.
- Q41b *Source: Original; new.* Acupuncture is thought to be a very rare route of infection acquisition.

We would like to rule-out this as a likely route of recent infection.

- Q42a *Source: Original; new.* Needle stick injuries have a high potential for causing transmission of infection and so this question will assess whether needle stick injuries have been the source of infection in any confirmed positive subjects in our study.
- Q42b *Source: Original; new.* Needle stick injuries have a high potential for causing transmission of infection and so this question will assess whether recent needle stick injuries have been the source of infection in any confirmed positive subjects in our study. As with other question the results of testing must be consistent with a recently acquired infection for a recent needle stick injury to be the potential route of acquisition.
- Q43a *Source: Original; new.* This risk factor has not been sufficiently assessed in previous studies and we would like to rule-in or rule-out this as a likely route of infection acquisition in blood donors.
- Q43b *Source: Original; new.* This risk factor has not been sufficiently assessed in previous studies and we would like to rule-in or rule-out this as a likely route of recent infection acquisition in blood donors.
- Q44a *Source: Original; new.* Family history is an important factor associated with the risk of hepatitis acquisition. To the best of your knowledge, has anyone living in your household (including family or roommates) been infected with Hepatitis B virus or Hepatitis C virus?
- Q44b *Source: Original; new.* This question is designed to determine if vertical transmission of infection is evident in family. This is one of the primary routes of HBV spread in persons from Southeast Asia.
- Q45a *Source: Original; new.* Family history is an important factor associated with the risk of HTLV acquisition. HTLV is known to have geographic foci of infection and so familial heritage is important to know for this infection.
- Q45b *Source: Original; new.* This question is designed to ascertain which family members are from areas known to be endemic for HTLV I or II.
- Q46a-e and Q47 *Source: EuroQol 5 Dimension Quality of Life questionnaire.* These questions must be used verbatim and together in order to have validity and comparability to other population-based studies of quality of life. This set of questions are analyzed together to develop an overall quality of life score. The EQ-5D is being used to determine if there are differences in the overall quality of life between confirmed positive and false positive donors. It is expected that quality of life will be lower for confirmed positive donors compared to controls and that HIV may have the lowest perceived quality of life. However quality of life in blood donors has not been measured in the US and so the expected patterns are speculative. We need to measure quality of life and this study will be the largest to do in blood donors in the US. This question will also permit us to understand if there are different impacts of testing positive for the different infections of interest in this study.
- Q48 *Source: Original; new.* This question is designed to assess if donors have chronic fatigue syndrome (CFS), which has recently and controversially been associated with a new virus named XMRV. XMRV may be transfusion transmitted and so this question will help us understand how common CFS is the donor population. All study subjects will be asked this question. It is particularly important for false positive donors to see if we can estimate the prevalence of CFS in

donors.

- Q49 *Source: Original; new. Source: Original; new.* This question is designed to assess if donors have fibromyalgia, which is similar to CFS. All study subjects will be asked this question. It is particularly important for false positive donors to see if we can estimate the prevalence of fibromyalgia in donors without other infections.