Supporting Statement A for

HIV Study in Blood Donors from Five Chinese Regions

OMB Number: 0925-0596

Reinstatement with Change

October 2014

Sponsored by:

The National Heart, Lung, and Blood Institute
Transfusion Medicine and Cellular Therapeutics Branch
National Institutes of Health

Project Officer/ICD Contact: Simone Glynn, MD
Transfusion Medicine and Cellular Therapeutics Branch

Division of Blood Diseases and Resources
National Heart, Lung, and Blood Institute
Two Rockledge Center
Suite 9142
6701 Rockledge Drive
Bethesda, MD20892
Phone: (301) 435-0065
Fax: (301) 480-0868
Email: glynnsa@nhlbi.nih.gov

TABLE OF CONTENTS

ATTACHMENTS

SUPPORTING STATEMENT

Introduction and Summary

This Study is a reinstatement with change of OMB Number: 0925-0596 expiration date, January 31, 2012. The complete set of changes from the previous OMB approved study are described in Sections A.6 and A.15, and are limited to the respondent questionnaire contents and a change in the incentive amount. To better understand the diversifying and changing Human Immunodeficiency Virus (HIV) epidemic, and contemporary HIV risk factors, especially those associated with recent HIV infections, this HIV risk factor study in China is proposed as part of the Recipient Epidemiology and Donor Evaluation Study-III (REDS-III) China program. The major objectives of the program will be to evaluate the proportion of blood donors in China who were tested positive for HIV and have acquired their infection recently or more remotely; the risk of releasing a blood product that contains HIV (HIV residual risk); and the risk factors associated with HIV infection in China. The program will also assess the frequency of distinct HIV-1 viral lineages and drug resistant mutations among HIV-positive blood donors. In 2011, there were 780,000 people infected with HIV in China and it is estimated that over 300,000 HIV infected people in China are not aware of their infection status (http://www.unaids.org.cn/pics/20130521161757.pdf). The large migrating population and the complexity of HIV transmission routes in China make it difficult to implement a comprehensive and effective national HIV control strategy. Risk factors for infections can change over time; thus, identifying factors that contribute to the recent spread of HIV in a broad cross-section of an otherwise unselected general population, such as blood donors, is highly important for obtaining a complete picture of the epidemiology of HIV infection in China. Because the pace of globalization means infections can cross borders easily, as suggested by recent HBV and HCV data from US CDC (http://www.cdc.gov/immigrantrefugeehealth/guidelines/domestic/hepatitis-screening-guidelines.html), the program objectives have direct relevance for HIV control in the US and globally. The proposed HIV risk factor study which is the subject of this OMB submission aims at identifying the risk factors that may be associated with the current transfusion-transmission of HIV.

A.1. Circumstances Making the Collection of Information Necessary

Under Title 42 › Chapter 6A › Subchapter III › Part C › Subpart 2 › § 285b–1 the Director of the National Heart, Lung and Blood Institute (NHLBI) shall conduct and support programs for the prevention and control of heart, blood vessel, lung, and blood diseases. Such programs shall include community-based and population-based programs carried out in cooperation with other Federal agencies, with public health agencies of State or local governments, with nonprofit private entities that are community-based health agencies, or with other appropriate public or nonprofit private entities. The proposed study, HIV Study in Blood Donors from Five Chinese Regions, fits within the NHLBI's research agenda as described here and in the other supporting documents.

The HIV Study in Blood Donors from Five Chinese Regions includes three components: 1) estimation of HIV prevalence and incidence in blood donors by demographics; 2) an evaluation of the genetic characteristics of HIV infections in blood donors; and 3) an evaluation of the relative prevalence of risk factors in HIV-positive blood donors.

Estimation of HIV risks: The estimated number of annual donations from the five blood centers participating in REDS-III studies (located in the cities of Urumqi, Luoyang, Mianyang, Liuzhou, and Chongqing) is 350,000. Blood donors are routinely tested for transfusion-transmissible infections including HIV , hepatitis B (HBV) and hepatitis C (HCV) when they present to donate. These test result data as well as donor demographic information collected by the five blood centers for operational purposes will be analyzed to evaluate HIV as well as HBV and HCV prevalence, incidence, and residual risk (the risk of a blood donation containing HIV, HBV, or HCV being released in the blood supply). In the past, the rate of repeat donation by blood donors in China was very low and there was no longitudinal follow-up of donations from the same donors. Recent years have seen an increase in blood donations from repeat donors in most Chinese regions. This increase permits longer-term follow-up and testing of repeat donors which allow for calculation of HIV incidence rates and residual risks. This program component will be achieved through analysis of existing operational blood donation data from participating blood centers as well as the results from the additional testing of blood specimens that will have been collected as part of the normal blood collection processes at the blood centers. There will be no involvement of research subjects or respondents in this program component, and thus no additional burden.

Evaluation of the genetic characteristics of HIV infections in blood donors: This study will also monitor genetic characteristics of recently acquired infections through genotyping and drug resistance testing, thus serving a US and global public health imperative. The monitoring of drug resistance patterns in newly acquired infection is critical to determine if currently available antiretroviral medicines are capable of combating infection. Genotyping and host response information are scientifically important not only to China, but to the US and other nations since they provide a broader global understanding of how to most effectively manage, control, and potentially prevent HIV, for example through vaccine development. Efforts to develop vaccines funded by the National Institutes of Health and other US-based organizations may directly benefit from the findings of this study. This program component will be achieved through additional testing of blood specimens that will have been collected as part of the normal blood collection processes at the participating blood centers. There will be no involvement of research subjects or respondents in this program component, and thus no additional burden.

Evaluation of the prevalence of risk factors in HIV-positive blood donors: This third component of the study is a case-control study. This study will be conducted over a 2 and 1/2 year period to evaluate the risk factors associated with HIV infection among blood donors using a questionnaire. Cases will be defined as donors who deny risks on the donor screening questionnaire prior to making a donation but are found to be positive on HIV testing of their donation (their donation is discarded). HIV-positive donors who gave blood at one of the five blood centers as stated above (primary sites) or at blood centers located in the Guangxi Autonomous Region (peripheral sites, recruited through the Guangxi CDC for this study only but not other REDS-III studies) will be eligible to participate and complete a Risk Factor Questionnaire that will assess general demographic and risk factor information pertinent to HIV infection. Controls will be those donors whose blood screens reactive for anti-HIV-1/2 but negative for HIV on Western blot confirmatory testing. A negative confirmatory test indicates that the donation (donor) is negative for HIV (false positive screening test result). Assuming a 50% or a 33% response rate, it is anticipated that 390 or 256 HIV-positive donors and 960 or 633 controls will participate in the case control study, respectively. The HIV risk factor study will estimate the relative prevalence of HIV risk factors among blood donors and help develop more effective donor behavioral screening policies to prevent window period infections (those recently acquired infections that are not detected by the donor screening tests) and improve the safety of

the blood supply. This HIV risk factor study will enroll blood donors and completing the questionnaire by enrolled blood donors will impose a burden on respondents.

Taken together, the results of the three components of this study will provide a broader global understanding of HIV epidemiology, and support public health efforts to most effectively manage and potentially prevent HIV transmission in China, and globally. While all three components are included in the study protocol and also referenced in this supporting statement to allow for the proposed HIV risk factor study to be put in the appropriate context, this request for OMB review is only for the HIV risk factor study that will enroll blood donors and survey the enrolled donors for various risk factors that may be associated with HIV transfusion-transmission.

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 investigations in Brazil and China. Continuing this effort, the goal of the REDS-III International Component is to conduct epidemiologic, laboratory, and survey research on blood donors in selected countries in regions seriously affected by the AIDS epidemic to help increase the safety and availability of blood for transfusion. Specific objectives for the REDS-III International program 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.

The REDS-II program evaluated HIV risk factors among 77 HIV-positive blood donors who donated blood at Kunming, Luoyang, Mianyang and Urumuqi between 2009 and 2011. This study was small, and while providing useful baseline information, does not provide for a contemporary evaluation of risk factors in Chinese blood donors in the face of a rapidly evolving epidemic and changing blood donor screening practices. Consequently, after the RED-II study was completed and data were analyzed and studied, these study investigators collaborated to develop a protocol for a more comprehensive HIV study of risk factors in Chinese blood donors under REDS-III. This proposed study will be larger, collecting data from more blood centers and thus increasing the study's geographic representation. Further, this study will provide up-to-date information on the relative prevalence of risk factors in blood donors who denied risk factors on the donor history questionnaire. In REDS-II, we recruited 77 HIV positive donors, a sample size probably too small to capture emerging risk factors for HIV. The proposed study will allow for a better understanding of the diversifying and changing HIV epidemic, and the current risk factors, especially those associated with recently-acquired HIV infections. Recently infected donors pose greater risk for blood safety due to their seemingly good health status and higher likelihood of being in the window period of HIV infection when donating, a period when the HIV infection is not detectable by current blood donation testing. These donors also most closely represent the current infections routes and risk behaviors in China. By linking the risk factor information to the HIV test data, and donor demographic characteristics, and comparing these data with the data obtained in the REDS-II study, we will be able to establish the profiles of recently HIV infected donors and possibly identify new strategies to prevent window period blood donations from high risk donors.

A.3. Use of Information Technology and Burden Reduction

For this HIV risk factor study, donors whose donations test reactive on the HIV antibody screening tests that are being used at blood centers in China will be contacted via phone, informed about the study, and, if consenting to participate, given an option to complete a paper survey and mail it back or to use a web based survey tool to submit their responses. In some blood centers and as authorized by their local Centers for Disease Control (CDC) (e.g., Luoyang Blood Center), consenting HIV reactive donors will have the option to complete the survey (called the Risk Factor Questionnaire) in a private room during their visit to the blood center.

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

Similar research is being conducted in other social groups such as sex workers in China. However, this study is unique as it builds upon information learned from the REDS-II Risk Factor Survey, and there is no other research being conducted to study viral risk factors in the broader Chinese blood donor community.

A.5. Impact on Small Businesses or Other Small Entities

Small businesses or entities are not involved. All respondents are individual blood donors.

A.6. Consequences of Collecting the Information Less Frequently

The survey or Risk Factor Questionnaire will be administered only once. The Risk Factor Questionnaire is similar to the one that was used during the REDS-II study to assess risk factors for HIV with a few new components addressing the new epidemiological features as reported about the general population. One new section inquires about the risks associated with injection in county-level hospitals, village clinics, and private clinics where standard sanitation requirements may not be followed. Another new section asks about risks associated with migrant workers who are an important part of the donor pool but are at high risk for sexually transmitted diseases and serve as an important transmission route between metropolitan and rural regions as well as high-risk to low risk populations. A few other modifications include more specific questions about hetero- and homo-sexual partners and sexual behaviors given the increasing importance of sex as a major transmission route in the general population. As stated above, due to available technology for identification of recent HIV infection and the changes in the donor screening questionnaire, it is important to collect this new information. The questionnaire will also collect general demographic and risk factor information pertinent to the HIV virus.

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 in Volume 79, Thursday, June 12, 2014, on page 33764. One public comment was received that was a personal opinion regarding conducting research about the Chinese blood donation system. There has been consultation outside of NHLBI to conceptualize and design the proposed study. The final study design was developed, reviewed, and approved by the REDS-III China Program Steering Committee (Attachment 5.4), the REDS-III Executive Committee, the International Advisory Committee (Attachment 5.3) for the overall REDS-III study, and the Observational Study Monitoring Board (OSMB) (Attachment 5.1). The OSMB reviewed the final protocol and provided input and comments. Revisions were made to the protocol incorporating the suggestions of the OSMB.

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

A 100 Yuan (equivalent to 15 US dollars) monetary reward will be provided for completing the survey. Online survey completion will prompt local blood centers/Guangxi CDC to issue the incentive either in the form of cash to be picked up by individuals at the local CDC or local blood centers, coupon codes for phone charge through phone call or text message, or a check or paper coupons in the mail of the same value. This monetary reward structure is consistent with the study's previous data collection under the same OMB number as the previously approved study.

A.10. Assurance of Confidentiality Provided to Respondents

The REDS-III consent forms that will be given to all donors will explain that all study information entered into the REDS-III China database, and submitted to REDS-III Data Coordinating Center (RTI, NC, USA) will be identified only with a study ID, i.e., without any of the donor's personal information. The study ID is generated for the REDS-III China program using an irreversible process. A link between the Study ID and the donor personal information is only maintained by the blood center without any access of the other study personnel outside of the blood center.

Detailed final study protocols have been approved by the IRB at JHU and by the Ethical Committees at IBT, the Chinese Institute of Blood Transfusion in China. All measures will be implemented to protect the privacy of all the study participants by maintaining a secure database. All study personnel will be trained and certified using the materials provided by JHU's Office of Research Administration on human subject protection in research. Only research staff at the blood centers will have access to donor personal identification information needed for the follow-up contact. All data and samples will be identifiable by the Study ID only before submitted to IBT and the REDS-III Data Coordinating Center.

The following will be the REDS-III China donor and donation identification procedure: Standardized donor and donation data forms will be used at all blood collection sites to document donor and donation information. The standard data form used by the blood centers will show a donor's name and contact information (including address and phone number), a unique REDS-III China Study Identification number (Study ID), and donor and donation information required for REDS-III. All donor and donation information that will be transferred to REDS-III DCC, will only be identified by the REDS-III China Study ID, with no personal identification information including donor names, contact information, and other unique private identification

information (such as citizen identification number). The link between a donor's identity and Study ID will be maintained only at the blood center and will not be available to any other REDS-III study personnel. The Privacy Act does not apply to the proposed data collection since identifiable information will not be collected on this questionnaire.

A.11. Justification for Sensitive Questions

As noted in the beginning of this document, the questionnaire being used is nearly identical to the one that was developed for this study's previously approved collection effort (OMB Number: 0925-0596; expiration date, January 31, 2012), The few modifications are described in Section A6, and were based on a thorough review of the current international and Chinese literature. Efforts were made to ensure that the questionnaire is comprehensive and culturally appropriate. The questionnaire has been translated into Chinese and Uyghur languages. The Uyghur translation will be used for Uyghur donors in Urumqi, Xinjiang. The purpose of the interview questionnaire is to collect donor profile data for comparing risk exposures between blood donors who test HIV positive (cases) and HIV false-positive (controls).

Donations that have false positive results for HIV on ELISA screening (Western blot confirmed negative) have been shown to be negative for HIV on follow up tests (based on in-house data from the REDS-III in-country laboratory at the Institute for Blood Transfusion or IBT) and the Chinese CDC in general does not send notification to these donors nor contact them for follow up evaluation.

The demographic information collected will include gender, birth year, ethnicity, current occupation, level of education, and marital status. Previous donation history questions will be used to collect data about the frequency of previous donation and the year and type of each blood donation. In China due to the unsanitary illegal blood collections of the early to middle 1990s, the history of plasma donation in the 1990s has been identified by several studies as a major risk factor for HIV infection in certain regions. So these questions will capture information on the association between previous donation and HIV infection status.

To determine motivational factors that lead participants to donate blood, there are questions related to incentives and motivation. These questions will help evaluate how often blood donors donate to get their blood tested (test seeking). Blood bank serology testing may be a magnet that attracts people with risk factors wishing to be tested**.** We intend to ascertain donor's perceptions/confidence related to viral serology performed by the blood bank as well as whether seeking blood screening serology testing was a contributing factor in a donor's motivation for donating.

Medical history questions will be used to obtain data related to general medical history exposures that could lead to viral transmission, including acupuncture, medical injection, medical surgery, cosmetic surgery, dental cleaning, dental surgery, endoscopies, both life time and exposure 6 months before blood donation.

Previous deferral information will be collected to ascertain if the blood donor has been deferred at the time of the blood donation and the reason for deferral. In China, the blood centers are building up the information system for deferred donors to allow for automatic identification of deferred donors who may attempt to donate again. These survey questions will be useful for understanding the effectiveness of this deferral system, to evaluate the donor's recollection on being deferred and reason for the deferral, and on the motivation for current donation.

The "Previous diagnosis section" will ask questions about the donor's previous diagnosis of hepatitis, HIV and sexually transmitted diseases as well as the infectious status of their family members. Drug use questions will be asked to evaluate the influence of illicit drug use on viral

infections. The questions include injected and non-injected illegal drugs use and frequency. To ascertain if illegal drug use including sharing the drug delivery device could lead to disease transmission, we also ask the questions about sharing of an injected drug delivery device.

The sexual lifestyle questionnaire items are used to obtain data related to donor's sexual practice, including the number of sexual partners during lifetime and in the past 6 months and whether having more sexual partners increases the odds of having HIV as well as its spread – HIV can be transmitted both through blood and sexually. The sexual history will also allow us to determine the prevalent sexual behavior patterns among high-risk Chinese blood donors and whether this pattern may or may not be correlated with specific serologic markers. A better understanding of sexual risk factors for HIV may allow us to build more effective questions to improve the donor selection process. It may also help us to avoid potential discrimination and unnecessary loss of donors if the patterns of viral transmission are not shown to be associated with certain sexual activity.

Work place exposure questions are included based on the assumption that the donors who work in a health care profession or other social setting that could lead to exposure to blood or other body fluids could be at higher risk for HIV acquisition. To obtain data related to rare risk factors for HIV infection such as body piercing and tattoo, we ask about lifetime exposure and also more specifically about exposure 6 months before blood donation.

Questions will be included to determine the donor testing notification service provided by the blood center and whether or not the donor is willing to adhere to the advice for further testing and health care. This will help us understand if the notification process is effective.

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

The estimated annualized burden hours 450 will be for 1,350 respondents and the cost to respondents is estimated at $1,030.5 based on $2.29 per hour. It is estimated that each respondent will spend about 2 minutes to complete the informed consent and 18 minutes to complete the questionnaire. According to China's National Bureau of Statistics in 2013, the average annual wage in China is 29,547 Chinese Yuan (or $ 4,765.65 US dollars based on current exchange rate of 1 US dollar = 6.2). http://www.stats.gov.cn/tjsj/ndsj/2013/indexeh.htm

Table A.12-1: Estimated Annualized Burden Hours

Form Name	Type of Respondents	Number of Respondents	Number of Responses per Respondent	Average Burden Per Response (in hours)	Total Annual Burden Hours
HIV Risk factor Q	Blood donors – Case Primary Sites	210	1	20/60	70
	Blood donors – Case peripheral sites	180	1	20/60	60
	Blood donors			20/60	

	-Control primary sites	540	1		180
	Blood donors –Control- peripheral sites	420	1	20/60	140
	Blood donors - total	1,350	1	20/60	450

Table A.12-2: Estimated Annualized Burden Costs

Form Name	Number of Respondents	Frequency of Response	Average Time per Respondent	Hourly Wage Rate *	Respondent Cost
HIV Risk factor Q (Case - Primary Sites)	210	1	20/60	$2.29	$160.3
HIV Risk factor Q (Blood donors – Case peripheral sites)	180	1	20/60	$2.29	$137.4
HIV Risk factor Q (Blood donors - Control primary sites)	540	1	20/60	$2.29	$412.2
HIV Risk factor Q (Blood donors – Control- peripheral sites)	420	1	20/60	$2.29	$320.6
Blood donors - total	1,350	1	20/60	$2.29	$1,030.5

*****http://www.stats.gov.cn/tjsj/ndsj/2013/indexeh.htm

A.13. Estimates of Other Total Annual Cost Burden to Respondents or Record Keepers

There are no capital or start-up costs, and no maintenance or service cost components to report.

A.14. Annualized Cost to the Federal Government

The annualized cost to the Federal Government for the proposed study is estimated to be approximately $ 203,999 per year for each of three years.

Item	Salary	Fringe Rate (%)	% Effort	Annualized Data Collection Cost
NIH Project Oversight Officer - GS15-10	157,100	20	1.5	23,565
4 in-house contractor staff	125,944	39	30.8	38,853
3 in-house contractor staff	14,542	7	38.5	14,689
10 of field contractor staff	8,658	7	100	68,551
Operational Costs for Data Collection Activities – Printing, equipment, overhead), non-labor				42,742
Other Contractual costs for data collection, non-labor				2,466
Travel costs associated with data collection				13,133
Other costs, non-labor				0
Total				203,999

A.15. Explanation for Program Changes or Adjustments

This HIV Risk Factor Survey constitutes a request for a reinstatement with change of a previous collection of information (OMB Number: 0925-0596 expiration date, January 31, 2012). Compared with the previous study, there are three changes:

1. Increased number of study sites from four to five: the previous study was conducted with blood donors at four blood centers (Kunming, Luoyang, Mianyang and Urumqi), while the current study collects data from a larger number of blood centers (Chongqing, Guangxi, Luoyang, Mianyang and Urumqi) thus increasing the study's geographic representation.

2. New survey questions to examine recently HIV infected donors: the questionnaire includes new questions about potential risk factors that may be associated with recently-acquired HIV infections and new questions probing detailed risks associated with increasing HIV prevalence in high risk groups. With this information captured and linked to the HIV test data and donor demographic characteristics, the study aims to establish the profiles of recently HIV infected donors and possibly identify new strategies to prevent window period blood donations.

3. Decrease amount of incentive for survey participants from 200 RMB to 100 RMB: based on the data collection team's experience with conducting similar surveys with this population in these regions in China, it was decided that this study does not need 200 RMB incentive.

A.16. Plans for Tabulation and Publication and Project Time Schedule

The schedule for study activities is shown in Table A.16.

Table A.16: Study Timeline

Activity	Time Schedule
Donor Enrollment	January 1, 2015
Study Completion	June 30, 2017

Subject to NHLBI review, data will be disseminated to the scientific and blood banking community and others through peer-review journal publications, and presentations at government (FDA Blood Products Advisory Committee) and professional meetings (American Association of Blood Banks).

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

The OMB expiration date will be displayed in the upper-right hand corner of the questionnaire.

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

There are no exceptions to the certification statement of OMB Form 83-I.