[NIH Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Proposed Collection; 30-day comment request

Incident HIV/ Hepatitis B virus infections in South African blood donors: Behavioral risk factors, genotypes and biological characterization of early infection

SUMMARY: Under the provisions of Section 3507(a)(1)(D) of the Paperwork Reduction Act of 1995, the National Heart, Lung, and Blood Institute (NHLBI), the National Institutes of Health (NIH) has submitted to the Office of Management and Budget (OMB) a request for review and approval of the information collection listed below. This proposed information collection was previously published in the Federal Register in Volume 78 on Friday, November 8, 2013, and page 67175, and allowed 60-days for public comment. One public comment was received that was a personal opinion regarding protecting the safety of the American blood donation system. The purpose of this notice is to allow an additional 30 days for public comment. The National Institutes of Health may not conduct or sponsor, and the respondent is not required to respond to, an information collection that has been extended, revised, or implemented on or after October 1, 1995, unless it displays a currently valid OMB control number.

DIRECT COMMENTS TO OMB: Written comments and/or suggestions regarding the item(s) contained in this notice, especially regarding the estimated public burden and associated

response time, should be directed to the: Office of Management and Budget, Office of Regulatory Affairs, OIRA_submission@omb.eop.gov or by fax to 202-395-6974, Attention: NIH Desk Officer.

COMMENTS DUE DATE: Comments regarding this information collection are best assured of having their full effect if received within 30 days of the date of this publication.

FOR FURTHER INFORMATION: To obtain a copy of the data collection plans and instruments or request more information on the proposed project contact: Simone Glynn, MD, Project Officer/ICD Contact, Two Rockledge Center, Suite 9142, 6701 Rockledge Drive, Bethesda, MD 20892, or call 301- 435-0065, or E-mail your request, including your address to: glynnsa@nhlbi.nih.gov. Formal requests for additional plans and instruments must be requested in writing.

PROPOSED COLLECTION: Incident HIV/ Hepatitis B virus (HBV) infections in South African blood donors: Behavioral risk factors, genotypes and biological characterization of early infection, 0925-New, the National Heart, Lung, and Blood Institute (NHLBI), the National Institutes of Health (NIH).

Need and Use of Information Collection: South Africa has one of the highest burdens for HIV infection in the world. The HIV epidemic in South Africa is largely heterosexual, but risk factors for infections can change and so identifying factors that contribute to the recent spread of HIV in a broad cross-section of the otherwise unselected general population, such as blood donors, is highly important for obtaining a complete picture of the epidemiology of HIV

infection in Africa. Small previous studies suggest that the risk factors for HIV among more recently acquired (incident) infections in blood donors may differ from those of more distant (prevalent) infections. Similarly risk factors for recently acquired HBV may be different than for prevalent HBV infections. The demographic and behavioral risks associated with incident HIV and incident HBV infection have, as yet, not been formally assessed in South African blood donors using analytical study designs. Due to the high rates of HIV and HBV infection in South African blood donors, a better understanding of these risk factors can be used to modify donor screening questionnaires so as to more accurately exclude high-risk blood donors and contribute to transfusion safety. Risk factor data from this research may also provide critical information for blood banking screening strategies in other countries.

This study which provides a contemporary understanding of the current risk profiles for HIV and separately for HBV will also prospectively monitor genetic characteristics of recently acquired infections through genotyping and drug resistance profile testing, thus serving a US, South African, and global public health imperative to monitor the genotypes of HIV and HBV that have recently been transmitted. For HIV, the additional monitoring of drug resistance patterns in newly acquired infection is critical to determine if currently available antiretroviral medicines are capable of combating infection. Because the pace of globalization means these infections can cross borders easily, these study objectives have direct relevance for HIV and HBV control in the US and globally. Further, the ability to identify recent HIV infections provides a unique opportunity to study the biology, host response and evolution of HIV disease at time points proximate to virus acquisition. Genotyping and host response information is scientifically important not only to South Africa, but to the US and other nations since it will provide a broader global understanding of how to most effectively manage and

potentially prevent HIV (e.g. 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.

The South African National Blood Service (SANBS) uses both individual donation Nucleic Acid Testing (ID-NAT) and serology tests (either antibody or antigen detection tests) to screen blood donors for HIV and Hepatitis-B Virus (HBV), among other infections. A positive NAT test precedes HIV antibody detection or HBV surface antigen detection by days to weeks in newly acquired HIV and HBV infections. A combined testing strategy using NAT and serology tests therefore confers the ability to detect most acute infections and discriminate between recent (incident) and more remotely acquired (prevalent) infection. Additional tests that exploit antibody maturation kinetics such as the HIV Limiting Antigen Avidity assay (LAg Avidity) can further assist to classify persons with an HIV antibody positive test as having a recently acquired (incident) or longer-term (prevalent) infection. Hepatitis B core antibody (anti-HBc) testing of NAT-positive and NAT and Hepatitis B Virus Surface Antigen (HBsAg) positive HBV infections allows classification of HBV infections as recently acquired or prevalent infections. Infections that are anti-HBc negative are recently acquired (incident).

Leveraging this ability to classify HIV and HBV infections as incident or prevalent leads to three study objectives:

1. Objective 1 consists of evaluating the risk factors associated with having an incident HIV or HBV infection. To that end, a frequency matched case-control study will be conducted with two case groups: incident HIV infected blood donors and incident HBV infected blood donors, respectively. Risk factors in these two case groups will be compared to the

risk factors provided by a group of controls (blood donors whose infectious tests are all negative). Cases and controls will be accrued from a geographically diverse donor pool.

2. Objective 2 consists of characterizing HIV clade and drug resistance profiles and determining viral loads in all cases of incident HIV infection, as well as characterizing HBV genotype and viral load in all incident HBV infections.
3. Objective 3 consists of following persons with incident and "elite controller" HIV infections prospectively for three additional visits at 2, 3, and 6 months following the index positive test(s). The term "elite controllers" refers to those who are HIV antibody positive, but with undetectable viral RNA (NAT negative) who are believed to have a natural ability to control viral replication without therapy. These studies will be useful in identifying appropriate HIV drug therapy regimens for this condition, as well as strategies for producing an effective HIV vaccine, which has eluded 30 years of HIV research.

OMB approval is requested for 3 years. There are no costs to respondents other than their time. The total estimated annualized burden for Objectives 1 and 2 will be 395 hours for 483 respondents (participants). The total estimated annualized burden for Objective 3 will be 32 hours for 35 respondents.

Form Name	Type of Respondent	Number of Respondents	Number of Responses per Respondent	Average Burden Per Response (in hours)	Total Annual Burden Hour
Objectives 1 and 2 consent form	Adult Donors	483	1	15/60	121
Objectives 1 and 2 – ACASI	Adult Donors	483	1	34/60	274

Questionnaire					
Objective 3 consent form - Year 1	Adult Donors	35	1	15/60	9
Objective 3 – Clinical Follow-up Questionnaire – Year 1 *	Adult Donors	35	4	10/60	23
Objective 3 consent form* - Year 2	Adult Donors	35	1	15/60	9
Objective 3 – Clinical Follow-up Questionnaire – Year 2 *	Adult Donors	35	4	10/60	23

* The Objective 3 respondents are a subset of the respondents included in Objectives 1 and 2.

Dated: February 3, 2014._____

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Keith Hoots,

Director, Division of Blood Diseases and Resources,

National Heart, Lung, and Blood Institute, NIH.

Dated: _February 6, 2014._____

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Lynn Susulske

NHLBI Project Clearance Liaison

National Institutes of Health

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