[NIH Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Proposed Collection; 60-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: In compliance with the requirement of Section 3506(c) (2) (A) of the Paperwork Reduction Act of 1995, for opportunity for public comment on proposed data collection projects, the National Heart, Lung, and Blood Institute (NHLBI), the National Institutes of Health (NIH), will publish periodic summaries of proposed projects to the Office of Management and Budget (OMB) for review and approval.

Written comments and/or suggestions from the public and affected agencies are invited on one or more of the following points: (1) Whether the proposed collection of information is necessary for the proper performance of the function of the agency, including whether the information will have practical utility; (2) The accuracy of the agency's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) Ways to enhance the quality, utility, and clarity of the information to be collected; and (4) Ways to minimize the burden of the collection of information on those who are to respond, including the use of

appropriate automated, electronic, mechanical, or other technological collection techniques or other forms of information technology.

TO SUBMIT COMMENTS AND FOR FURTHER INFORMATION: To obtain a copy of the data collection plans and instruments, submit comments in writing, 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.

COMMENTS DUE DATE: Comments regarding this information collection are best assured of having their full effect if received within 60 days of the date of this publication.

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 subjects. 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 Questionnaire	Adult Donors	483	1	34/60	274
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 1and 2.

Dated: October 23, 2013.

Keith Hoots,

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National Heart, Lung, and Blood Institute, NIH

Dated: October 24, 2013.

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National Institutes of Health

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