Network Epidemiology of Syphilis Transmission (NEST)

OMB 0920-18MY

Supporting Statement – Part A

Revision

July 10, 2018

Updated October 22, 2018

Alex de Voux, PhD
Project Officer

National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Division of STD Prevention
Epidemiology and Statistics Branch
Centers for Disease Control and Prevention
1600 Clifton Road NE, Mailstop US12-3
Atlanta, GA 30333

Voice: (404) 639-1203
Fax: (404) 471-2518
Email: adevoux@cdc.gov

NETWORK EPIDEMIOLOGY OF SYPHILIS TRANSMISSION

Section A.

Justification.

1. Circumstances Making the Collection of Information Necessary
2. Purpose and Use of the Information Collection
3. Use of Improved Information Technology and Burden Reduction
4. Efforts to Identify Duplication and Use of Similar Information
5. Impact on Small Businesses or Other Small Entities
6. Consequences of Collecting the Information Less Frequently
7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5
8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency
9. Explanation of Any Payment or Gift to Respondents
10. Protection of the Privacy and Confidentiality of Information Provided by Respondents
11. Institutional Review Board (IRB) and Justification for Sensitive Questions
12. Estimates of Annualized Burden Hours and Costs
13. Estimates of Other Total Annual Cost Burden to Respondents or Record Keepers
14. Annualized Cost to the Federal Government
15. Explanation for Program Changes or Adjustments
16. Plans for Tabulation and Publication and Project Time Schedule
17. Reason(s) Display of OMB Expiration Date is Inappropriate
18. Exceptions to Certification for Paperwork Reduction Act Submissions

EXHIBITS

Table 12.A Estimated Annualized Burden Hours
Table 12.B Estimated Annualized Burden Costs
Table 14.A Estimated Cost to the Government
Table 16.A Project Time Schedule

LIST OF ATTACHMENTS

1. Authorizing Legislation
2. 60 Day FRN
2a. Public Comments
3. Survey
3a. Justification for survey questions
3b. Data elements summary and source

4. Screener
5. Smartphone Survey
6. Consent Form
7. Project Personnel
8. CDC IRB Determination
9. Study protocol
10. Privacy Impact Assessment

• Goal of the study: The Network Epidemiology of Syphilis Transmission (NEST) study is designed to describe the social and sexual networks of men who have sex with men (MSM) at high risk for syphilis in the United States to better understand the epidemiology of syphilis beyond individual-level risk factors.

• Intended use of the resulting data: Data from NEST will be used to address knowledge gaps in the transmission dynamics and epidemiology of syphilis in the United States by characterizing the structure and composition of sexual networks of MSM at increased risk of syphilis. These data will describe how these sexual networks change over time and contribute to the transmission of syphilis. Findings from NEST will be used to develop and guide public health interventions to slow the spread of syphilis.

• Methods to be used: NEST will establish cohorts of MSM at high risk for syphilis and prospectively collect demographic, behavioral, and social and sexual network data from participants in select cities. MSM will be recruited using respondent driven sampling. Study participants will have up to nine in-person visits, 3 months apart. At each visit, a behavioral survey will be completed and specimens facilitating tests for sexually transmitted infections (STI) will be collected.

• The subpopulation to be studied: MSM who are at high risk for syphilis, at least 18 years of age, and residing within one of the three participating sites.

• How data will be analyzed: Descriptive statistics and multivariable analyses to assess the prevalence of and trends in: 1) prevalence and incidence of syphilis, 2) risk behaviors for syphilis and, 3) utilization of and access to syphilis prevention services. Network analyses to investigate the structure and composition of sexual networks and how network characteristics change over time.

A. Justification

1. Circumstances Making the Collection of Information Necessary

The Centers for Disease Control and Prevention (CDC), National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP), Division of STD Prevention (DSTDP), requests a 3-year approval for a new data collection entitled, *Network Epidemiology of Syphilis Transmission* (NEST), as part of a research study to collect complex sexual network data among gay, bisexual, and other men who have sex with men (MSM) at high risk for syphilis in the United States. NEST will address knowledge gaps in the epidemiology of syphilis among MSM. This research study is funded by CDC through a cooperative agreement and will be conducted at three sites (two universities and a local health department) in the United States, which applied voluntarily through a competitive application process. This activity is authorized under Section 301 (Sec. 241) of the Public Health Service Act.

The United States is currently experiencing an ongoing syphilis epidemic (CDC, 2015). Once on the brink of elimination, syphilis rates in the United States are higher than they have been in the last 20 years. Syphilis, if left untreated, can cause severe medical issues including stillborn babies, infertility, and severe neurologic and ocular complications including stroke, hearing loss, and blindness (CDC 2015, Woolston S, et al., 2016). MSM are disproportionately impacted by syphilis and the majority of incident cases of syphilis in the United States occur among MSM. Rates of syphilis among MSM continue to sharply increase despite the continued application of traditional syphilis control activities, such as screening and contact tracing. New public health interventions to stem the spread of syphilis are urgently needed. However, development of new public health interventions requires data on and an understanding of current and actionable factors influencing syphilis transmission among MSM, such as social and sexual network characteristics, sexual behaviors, and healthcare access and utilization. Such factors are not only currently poorly understood, but may also change over time and rapidly. In order to address these knowledge gaps, both longitudinal individual-level and longitudinal network-level data need to be collected among this population. The collection of complex, longitudinal sexual network data — in addition to more traditional individual-level data, such as demographics and individual-level sexual and social behaviors — will address some of the knowledge gaps in the transmission dynamics and epidemiology of syphilis among MSM in the United States and point towards effective public health interventions to slow the spread of syphilis.

The overall objective of NEST is to support the establishment of cohorts of MSM at high risk for syphilis and to prospectively collect behavioral, social, and sexual network data, and biological specimens for sexual transmitted infection (STI) testing. Study participants will attend study

visits every three months for a period of up to 24 months. NEST is a multi-site study, with a target enrollment of approximately 720 MSM aged 18 years and older from three geographic areas of the United States: (1) Chicago, Illinois, (2) Baltimore, Maryland, and (3) Columbus, Ohio.

At each study visit, study participants will be interviewed and biological specimens (blood, urine, a rectal swab, and a pharyngeal swab) will be collected to facilitate testing for syphilis, gonorrhea, chlamydia, and HIV. All behavioral data will be collected through completion of the NEST survey (**Attachment 3**) and submitted electronically directly to the CDC NEST data manager. All personal identifying information (e.g., name, address) collected on individual participants will be retained by the local NEST site, will not be collected on NEST data collection forms, and will not be transmitted to CDC.

2. Purpose of Use of the Information Collection

The purpose of the NEST study is to address knowledge gaps in the transmission of syphilis among MSM in the United States by exploring the role of dynamic sexual and social networks. For the past several decades, public health officials have relied on public health interventions for syphilis that either focused on individual-level risk factors or — for interventions that focused on sexual networks, such as contact tracing — evinced marginal success despite rudimentary understandings of sexual networks.

When conducting contact tracing (also referred to as partner services), public health investigative staff interview persons diagnosed with syphilis to ascertain names and contact information of recent sexual partners. Public health staff then attempt to locate, interview, and test the partners for syphilis (and other STI). While this contact tracing approach can be effective in some settings and populations (such as those with small, simple, and static sexual networks), this approach is likely much less successful in the setting of complex and dynamic networks. Indeed, traditional contact tracing has not been successful in recent years in controlling syphilis among MSM, who may have more complex and dynamic networks than other populations. For public health officials to modernize contact tracing (to focus limited public health resources most effectively) and/or develop new effective network-level interventions, substantial gaps in knowledge of the sexual networks of these men need to be addressed.

To address these gaps, NEST aims to collect data on domains such as: (1) sexual partner turnover or churn (e.g., changes in the set of partners reported by MSM at 3-month intervals and how frequently these changes occur), (2) differences in types of sexual activities that MSM engage in with different sexual partners, (3) sexual mixing patterns (e.g., differences in

race/ethnicity, age, and gender between MSM and their sex partners), and (4) the proportion of partners first met using mobile applications or sex-seeking websites. NEST aims to collect data on the degree to which partnerships, sexual behavior, sexual mixing patterns, and how men find partners changes over time and the speed at which they may change. NEST will also address important gaps in knowledge by collecting data on the degree to which these sexual behaviors and partnership patterns may be influenced over time by syphilis diagnoses or use of HIV pre-exposure prophylaxis (PrEP).

In addition to contact tracing, syphilis screening has been a foundation of public health syphilis control efforts. However, screening rates are suboptimal (even among MSM who regularly seek healthcare) and several barriers exist to successfully scaling-up screening for population-level syphilis control among MSM. Screening criteria (which rely on data from a relatively small number of static individual-level factors) may not be sufficient to identify most-at-risk persons, particularly, as is likely, risk changes over time. Yet even before providers can make decisions about screening, successful widespread screening requires that persons at risk for syphilis seek healthcare. Little is known about the degree to which healthcare seeking behaviors among MSM, and factors that influence healthcare seeking, change over time. NEST aims to collect data on these content areas. These data will directly inform public health interventions that efficiently leverage the healthcare infrastructure and thus rely on healthcare seeking behavior.

To craft effective and efficient public health interventions to prevent syphilis among MSM, the complex interplay of the above factors must be better understood. This is of particular importance in this current era of HIV PrEP. Utilization patterns of HIV PrEP may influence the dynamic structures of networks, sexual behaviors, and healthcare seeking behaviors over time. As PrEP continues to expand as a successful biomedical HIV prevention approach, longitudinal data are needed to understand patterns of PrEP usage among this population (e.g., consistent vs. intermittent PrEP use), associations between patterns of PrEP use and sexual behavior and/or nature of partnerships, and how PrEP may influence healthcare seeking, frequency of STI testing, and expanded access to STI care. Findings from NEST will inform the design of interventions to reduce the spread of syphilis.

There are three study awardees, two universities (Ohio State University and University of Illinois at Chicago) and one local health department (Baltimore City Health Department) in collaboration with a university (Johns Hopkins School of Medicine). The recruitment of study participants as well as the data collection activities will be carried out at university-affiliated sites including local health departments, community LGBT organizations, local STD clinics and HIV/AIDS care facilities. The three awardees competed for this cooperative agreement and were selected after an external objective review process was conducted in February, 2017. In

their applications, awardees documented extensive experience with the collection, management, and protection of private and sensitive data collected from study participants electronically, including sexual history data, and described protocols that they have already established locally in order to securely store study data. To address confidentiality risks, site primary investigators will determine which study staff need access to data. Background checks are performed on all staff prior to granting the staff members access to data and data collection application. Study staff will only be granted access to the data that they need to accomplish study-related activities. Access to all data will require a password that is carefully monitored by the site primary investigators. Sites will use secure, web-based applications for the electronic collection and management of research and clinical data. Collected electronic data will be stored on password-protected desktop computers in rooms with doors and functional locks. Electronic databases that are created and exported for data analysis will not contain any personally-identifying information (PII); in such databases, participants will be identified only by a unique study-assigned ID that does not contain PII. No individually-identifying data of any sort will ever be released or published. Local site investigators will have complete control over who can access the data and access to study data will restricted to the site research study team.

Before starting data collection, a short eligibility screener (**Attachment 4, pages 7–10 of Attachment 3**) will be administered to prospective study participants. If the prospective participant is determined to be eligible, consent will be obtained from the participant (**Attachment 6**). Once consent is obtained, data collection will begin and will include a baseline visit and follow-up visits every three months for a total follow-up period of up to 24 months. At each visit, participants will provide biological specimens (blood, urine, a rectal swab, and pharyngeal swab) to allow testing for syphilis, gonorrhea, chlamydia, and HIV. Participants will complete an electronic standardized survey on a tablet or computer. Transmission of electronic data using the tablet or computer will be submitted to a secure server where stored data will be encrypted. After transmission to the server, data entered into the electronic data application on the tablet or computer will be deleted. The survey includes questions about the participants' sexual network, individual behaviors, healthcare access, healthcare seeking, and demographics. The survey consists of 11 questionnaire modules with a range of 4 to 41 questions per module (**Attachment 3**).

A small subset of sexual behavior questions will be delivered to the participant closer to real time via a smartphone survey using a weekly format. The smartphone survey (**Attachment 5**) is a brief voluntary survey with a subset of questions based upon the participants' previous responses. Participants can respond to the brief smartphone survey at any time to record a sexual encounter. A weekly text message will be sent on Sunday nights with a reminder on Monday evening, to document sexual behavior in the last 24 hours. Smartphone surveys will be

delivered electronically as a text message notification to participants and each survey is expected to take 2 minutes. Data collected on electronic devices will be stored on a secure web-accessible local server at each of the three funded sites, which will only be accessible with a user name and password. Data security and privacy protections listed above also apply to data collected from the smartphone survey.

The primary study outcome is descriptive data on the composition and structure of sexual networks of MSM collected at each study visit and over the study period. These descriptive data include the average number of partners reported by MSM, the average age of partners reported, the proportion of partners reported who are male, and engage in specified risk behaviors. Furthermore, we will examine how different network structures may be associated with incident syphilis cases and the potential role of these networks in the transmission of syphilis. Additional outcomes include descriptive data on healthcare seeking, PrEP use, and attitudes toward PrEP over time.

Since few studies have collected complex sexual network data from MSM over time, we will evaluate participant recruitment and retention over the proposed 24-month follow-up period. We will quantify the response rates to sexual network questions over time and the proportion of participants lost to follow-up. Study staff at each site will plan to contact participants who are lost to follow up for a brief interview to ascertain the reasons for dropping out of the study and barriers to study participation that the participants may have experienced. As part of data analysis, we will describe demographic characteristics of participants who have dropped out of the study and compare these to retained participants to determine if there are any meaningful differences between these two groups.

3. Use of Improved Information Technology and Burden Reduction

In order to reduce the burden on study participants, the survey that participants are required to complete at each visit will be delivered electronically on a tablet or computer to minimize participant burden and improve usability. Relevant participant data (such as demographics) collected at prior visits will be uploaded securely ahead of the upcoming study visit interview, thereby minimizing the amount of data to be collected from participants at follow-up visits and reducing participant burden overall.

In order to reduce the burden on local site data managers, CDC will provide standardized SAS data structures with variable names, lengths and types defined for all requested datasets. To support the generation of high-quality analyzable data, local sites will need to complete data verification and validity checks on datasets prior to transmission to CDC. CDC will provide data check programs in order to facilitate this process and reduce the burden on the local data

manager. In collaboration with data managers at each participating site, CDC will provide data programs to local sites in order to ensure appropriate quality assurance. Sites will assure validity of data prior to transmission. Data will be uploaded every three months by trained data managers at collaborating sites. Wherever possible, automation will be utilized at the local level to significantly lessen the burden on collaborating staff.

4. Efforts to Identify Duplication and Use of Similar Information

CDC completed a thorough review of the literature, and there are no similar ongoing data collection activities conducting longitudinal evaluations of complex sexual network data among MSM at high risk for syphilis at either the national or regional level.

5. Impact on Small Business or Other Small Entities

Respondents include participants enrolled in the study, academic university-affiliated collaborators, and local health department collaborators. Data/information collection instruments have been held to the absolute minimum of questions required for intended use of the data/information, computer-based forms are used to simplify data collection, and respondents are permitted to report data electronically to reduce burden and improve data quality.

6. Consequences of Collecting the Information Less Frequently

Sexual networks of men who have sex with men (MSM) are dynamic and can change relatively rapidly over time. We are interested in how the composition and structure of the sexual networks change over time and how changing networks impact syphilis transmission, so it is important that we collect information to describe the sexual network every three months. We anticipate that initiation and discontinuation (and re-initiation) of HIV PrEP occurs over the course of weeks–months. Collecting data less frequently than quarterly will substantially hinder the ability of study investigators to address study objectives in a rigorous and valid manner.

There are no legal obstacles to reduce the burden.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

This request fully complies with the regulation 5 CFR 1320.5**.**

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

A 60-day notice was published in the Federal Register on March 5, 2018, Volume 83, Number 43, page 9318 (**Attachment 2**). CDC received one comment related to the previous notice in favor of the NEST project and the benefits of conducting the NEST study in order to reduce the spread of syphilis (**Attachment 2a**). No response was sent to the public comment posted. To date there have been no efforts made to consult outside the agency.

9. Explanation of Any Payment or Gift to Respondents

Tokens of appreciation will be used in NEST, as the project seeks to conduct surveys with a highly selective population and to ask them sensitive questions about sexual behaviors and substance use. Recruiting MSM at high risk for syphilis and HIV to participate in research studies has been shown to be difficult for reasons related primarily to the time burden and to fear of experiencing stigma. We expect the baseline and follow-up visit to take 90 minutes (including completion of the survey and collection of biospecimens — urine, pharyngeal swab, rectal swab, and blood). In order to increase response rates and retention over time, eligible persons will be offered a token of appreciation. Tokens of appreciation have been shown to increase response rates, which in turn improves the validity and reliability of the data (Abreu and Winters 1999; Shettle and Mooney 1999). We anticipate that the increased response rates and retention over time will lead to an improved representativeness of the underlying target population.

CDC will not provide these tokens of appreciation directly to study participants. Rather, each of the three funded sites will provide participants with tokens of appreciation to facilitate recruitment, participation, and retention. Participants will be given $50–$75 for completing each visit; amount and form (cash, gift cards, VISA cash cards) are determined locally based on local regulations, city characteristics (e.g., cost of living, average distance traveled to study site, form and cost of transport used to travel to the study site), and previous research experience with this specialized population. Each participant is expected to have a maximum of nine study visits during the course of the study.

In RDS methodology, participants also receive a token of appreciation when they successfully recruit one or more of their peers. Previous research has shown that providing a token of appreciation for recruiting a peer to the study increases peer recruitment and is an important aspect of RDS (Heckathorn, 1997). Participants will receive $15–$20 for each new participant they recruit into the study. Participants will also receive $3 for each weekly smartphone survey that they complete.

10. Protection of the Privacy and Confidentiality of Information Provided by Respondents

The Privacy Officer for CDC/ATSDR has assessed this package for applicability of 5 U.S.C. § 552a, and has determined that the Privacy Act does not apply to the information collection. CDC will not receive any personally-identifying information (PII). PII will be collected by participating sites (non-federal agencies) to permit contact of participants for follow-up visits only. Participants will also describe their recent sexual network and might provide names or nicknames of recent partners to the local study site interviewer. The secondary use of PII is to allow the local sites to track changes in sexual network structure and partnerships over time. The sites are non-federal agencies and are participating in the study as grantees of a cooperative agreement, rather than as recipients of a contract. Study sites will follow the processes that were determined by the local Institutional Review Boards (IRBs) to align with Health Insurance Portability and Accountability Act (HIPAA) requirements. Sites will not include PII in any datasets created for analysis or for transmission to the CDC. The CDC will not collect nor have access to patient names, medical record numbers, telephone numbers, home addresses, email addresses, or dates of birth. The CDC will treat information in a secure manner and will not disclose, unless otherwise compelled by law.

Study staff with approved access at local NEST sites will collect and have access to PII in order to contact participants for follow-up visits. Study staff will receive comprehensive training on the study protocol and standard operating procedures; protecting participant confidentiality; and cultural competency with racial/ethnic, gender and sexual minority populations. PII will be stored securely and separately from the collected study data (survey data, biological specimens, and STI test results) but will be locally linkable to collected study data using a unique study-assigned participant ID. The study-assigned participant ID will not contain any PII. PII will be retained for five years after completion of the study; study files containing PII will subsequently be destroyed and site investigators will provide attestation to the CDC project officer that data containing PII have been destroyed.

Site primary investigators will determine which study staff need access to data (and access will only be granted to the level of data required for their support of study activities). Background checks are performed on all staff before access to study data is authorized. Local staff will undergo data security and confidentiality training annually and will sign a confidentiality statement before access to study data is authorized. All study staff will be knowledgeable about local data security policies and procedures. Site investigators will ensure that the written data security policy is easily accessible. Access to all data will require a password that is carefully monitored by the site primary investigators. Electronic databases that are created and exported for data analysis will not contain any PII. The electronic data collection application supports electronic signature by positively identifying the user through a unique username and password

combination. Collected electronic data will be stored on password-protected desktop computers in rooms with doors with functional locks. Each site has fully a functioning Information Technology Systems (ITS) department that is responsible for maintaining its own web servers, database servers, file servers, firewall/networking, and desktop management. Sites will follow any additional local institutional policies regarding maintenance of participant confidentiality. Primary site investigators will have complete control over who can access the data that participants enter into the electronic data collection application and access will be restricted to members of the site study team. Once data are entered into the electronic data collection application, on password-protected computers or tablets, it will be transmitted to a secure server. Data that are stored on the secure server are encrypted. After transmission to the server, data entered onto tablets or computers will be deleted from the device. Network servers at each site are protected by network firewalls and all machines (desktop computers or laptops) at the site are protected by firewalling and have restricted access to ensure security compliance. All staff at local sites who have authorized access to the network server will abide by all applicable local laws, regulations, and policies. Information security protection practices in place at each site include:

- **User authentication system** relying on unique user names and passwords for system logon authentication and validation of the identity of users
- **Security tokens** for two-factor authentication for remote system access
- **Least privileged access** whereby each user is provided with a level of access to their personal computer that is adequate, but no higher than required, to accomplish the tasks that must be performed by that individual
- **Automatic time-out features** on systems requiring user re-authentication after prescribed intervals of inactivity
- **Regular anti-virus software updates and virus scans** managed by the site Information Technology Services (ITS) department.

In addition, study data may not be transferred or stored on personally-owned devices.

At CDC, only the NEST data manager and project coordinator have access to these de-identified data. The electronic NEST database will be stored on a CDC Information Technology Services Office (ITSO)-supported server housed in the Application Hosting Branch (AHB). This facility is protected by guards at the front gate entrance to the campus, inside the campus, and within buildings to control ingress and egress. Additional protections include Personal Identification Verification (PIV) card access to the building and rooms where the servers are located.

Data Transmittals and Safeguards

Data transmission from participating sites to the CDC will be restricted to CDC's Secure Access Management Services (SAMS). SAMS is an approved federal information technology system that provides authorized, validated users secure, encrypted access to CDC file transfer applications. The encrypted data will be stored in a secure CDC server with strictly controlled and restricted access rights.

The DSTDP Surveillance and Data Management Branch is charged with the responsibility of maintaining the privacy, security, and scientific integrity of all NEST databases. The Data Manager will be designated as the custodian of NEST data files and will be responsible for assuring all conditions of use and for security arrangements to prevent unauthorized use of, or access to NEST data. Access to the data shall be limited to specific DSTDP NEST staff members and designated collaborators of the study in the performance of their assigned duties.

The NEST Project Officer will be responsible for granting access to NEST data by other CDC staff in DSTDP as needed. The NEST collaborating sites will be promptly notified of any CDC personnel changes that affect access to the data for this project. All CDC personnel with data access have completed, and will remain current with, the annual Health and Human Services Information Security Awareness Training. A record of the completion of security training for all CDC staff is maintained by the CDC Information Technology Services (ITSO).

Local collaborators retain full control of and rights to analysis, research, and publication of their locally collected data.

Data Sharing Plan

Sites will comply with federal requirements for sharing research data. Data will be shared as directed by CDC. Sites will agree to:

- Publish their findings in a timely manner
- Deposit manuscripts into PubMed Central
- Provide summary data and other non-identifying information including protocols, data collection forms and publications to other investigators upon request. Investigators will be limited to those: a) working at an institution with a Federal-wide Assurance (FWA), and b) with appropriate expertise to analyze the data (e.g., possessing at least a master's degree in a related discipline).

All requests to use de-identified data will be evaluated by the NEST CDC study team and site primary investigators. These reviews will be conducted with special consideration to the privacy concerns of study participants, as well as scientific integrity and rigor of the data use proposal.

11. Institutional Review Board (IRB) and Scientific Justification for Survey Questions

IRB Approval

Local sites have all applied for IRB approval, two sites have received IRB approval and one site is currently undergoing IRB review. CDC has received a project determination stating that NEST is a research activity involving human subjects but that CDC involvement does not constitute engagement in human subject research (**Attachment 8**). Specifically, the project is funded under a cooperative agreement award mechanism and CDC employees will not intervene or interact with living individuals for research purposes, CDC employees will not obtain individually identifiable private information, and funded institutions have a Federalwide Assurance (FWA) and will be reviewed by a registered IRB linked to the FWA.

Scientific Justification for Survey Questions

A subset of data collected through the NEST survey (**Attachment 3**) are of a sensitive nature, including questions related to the patient's sexual behaviors, health insurance status, housing and food security, employment status, criminal justice involvement, and level of education attained. These data will be elicited from participants in a private environment. Many of the sensitive sexual behavioral questions are asked routinely during STI clinical care. Study staff will receive comprehensive training on interviewing techniques to build rapport and encourage participants' honest disclosure of sexual behavior and protecting participant confidentiality. These sensitive questions are essential in order to develop an accurate epidemiological assessment of syphilis in the community. These data are essential for understanding the epidemiology of syphilis and syphilis transmission. Justification for the NEST survey questions, including questions of a sensitive nature, are included in **Attachment 3a**.

12. Estimated Annualized Burden Hours and Costs

The respondents for the Network Epidemiology of Syphilis Transmission (NEST) study include (1) data managers at each of the three funded NEST study sites, and (2) participants enrolled in the NEST study at participating sites.

<u>NEST data managers</u>:
Every three months data managers from each of the three study sites will:

a) Manage and compile all study data collected from study participant visits that took place in the previous three months

b) Merge visit-specific clinical data from STI testing done on biological specimens with participant survey data (**Attachment 3b**)
c) Clean, recode, and structure data in accordance with NEST program guidance
d) Complete data verification and validity checks (per CDC NEST program guidance) on dataset prior to transmission to CDC, and
e) Transmit all data files to CDC through secure file transport mechanisms (SAMS)

We estimate that these data management processes will take approximately 10 hours for each of the three site managers with five data transmissions annually for a total of 150 annual burden hours.

Within three months of the end of each project year, the assigned data manager at each NEST site will compile, clean, validate and transmit an annual cumulative project dataset, including survey data, smartphone survey data, and STI testing laboratory data (**Attachment 3b**) to CDC through secure file transport mechanisms (SAMS) (for a total of 5 data transmissions per year). This final validated annual dataset from each site will be archived and become the primary repository for that site's annual reporting.

Participants enrolled in the NEST study:

NEST study staff will interview enrolled participants at a baseline visit and at follow-up visits every three months, for a total follow-up period of 24 months. Participants will therefore participate in a total of nine study visits over the 24-month study period. Each visit will include a questionnaire as well as collection of biological specimens (urine, blood, a pharyngeal swab, and a rectal swab) for STI testing. Each visit will take approximately 90 minutes per respondent for a total of 5, 400 burden hours annually.

Table 12A: Estimated Annualized Burden Hours

Type of Respondent	Form Name	No. of Respondents	No. of Responses per Respondent	Average Burden per Response (in hours)	Total Burden Hours
Potential participants	Screener; att 4	900	1	2/60	30
Site data manager	NEST data elements; att 3b	3	5	10	150
Study participants	NEST survey; att 3	720	5	1.5[a]	5,400

Study participants	Smartphone survey; att 5	720	52	2/60	1,248
Total					6,828

[a]Estimate for average burden per response (in hours) includes collection time for biological specimens (urine, blood, a pharyngeal swab, and a rectal swab).

The annualized burden cost is estimated in Table 12.B. below.

Hourly wages for the each of the two respondent categories were determined as follows:

- The mean hourly wage for NEST database administrators was estimated at a rate of $41.89. Estimates of hourly wage rates are based on the 2016 Bureau of Labor Statistics, National Occupational Employment and Wage Estimates for Database Administrators in the United States (accessed on November 14, 2017 at https://www.bls.gov/oes/current/oes151141.htm).
- The man hourly wage for participants enrolled in the NEST study was estimated at a rate of $23.86, which is the mean hourly wage reported on the 2016 Bureau of Labor Statistics, National Occupational Employment and Wage Estimates across all occupations in the United States (accessed on November 14, 2017 at https://www.bls.gov/oes/current/oes_nat.htm).

Table 12.B.Estimated Annualized Burden Costs

Type of Respondent	Form Name	Total Burden Hours	Hourly Wage Rates	Total Respondent Costs
Site data manager	NEST survey; att 3	150[a]	$41.89	$6,283.50
Study participant	NEST survey; att 3	5,400	$23.86	$128,844.00
Total		5,550		$135,127.50

[a]Estimate for burden hours includes collection time for biological specimens (urine, blood, a pharyngeal swab, and a rectal swab).

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

There will be no direct costs to the respondents other than their time to participate in each information collection.

14. Annualized Cost to the Federal Government

Funding is being made available through the CDC cooperative agreement (RFA-PS-17-002) over a total project period length of 3 years (May 1, 2017–March 30, 2020). The total annualized cost to the government is $2,724,241.20.

Table A.14: Estimated Annualized Costs to the Federal Government

Expense Type	**Expense Explanation**	**Annual Costs (dollars)**
Direct Costs to the Federal Government		
	CDC Data Manager (GS-13, .5 FTE)	$37,292
	CDC Laboratory Personnel (GS-15, .05 FTE)	$5,183.60
	CDC Laboratory Personnel (GS-14, .20 FTE)	$17,627.20
	CDC Laboratory Personnel (GS-13, .30 FTE)	$22,375.20
	CDC Epidemiologist (GS-13, .7 FTE)	$52,208.80
	CDC Project Coordinator (GS-14, .4 FTE)	$35,254.40
	Subtotal, Direct Costs to the Government	$169,941.20
Travel and other related expenses	Travel, and supplies	$ 54,300
	Subtotal, Travel and other project-related expenses	$ 54,300
Federal Grant	Understanding the Epidemiology of Syphilis in the United States research grant	$ 2,500,000
	Subtotal, Federal Grant	$2,500,000
	TOTAL COST TO THE GOVERNMENT	$2,724,241.20

15. Explanation for Program Changes or Adjustments

This is a new data collection.

16. Plans for Tabulation and Publication and Project Time Schedule

We anticipate initiation of data collection to be June 20, 2018. The project will continue through March 31, 2020. Preliminary data analysis is expected to begin 4–6 months after OMB approval. Additional data analysis will occur at least annually during the time period of the approved 3-year project period. Data analyses will include descriptive analyses and network analyses of sexual networks. Analyses of the data will be published in scientific and public health journals and presented at scientific meetings.

Table A.16: Project Time Schedule

Activity	**Time Schedule**
Collection of biological specimens and	Quarterly after OMB approval

clinical/demographic data from participating sites	
Data management and validation of data collected	Quarterly after OMB approval
Dissemination of results via annual report	12 months after OMB approval and annually thereafter

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

The display of the OMB expiration date is not inappropriate.

18. Exceptions to Certification for Paperwork Reduction Act (PRA) Submissions

There are no exceptions to the certification.

References

Abreu DA, Winters F. (1999). Using monetary incentives to reduce attrition in the survey of income and program participation. Proceedings of the Survey Research Methods Section of the American Statistical Association.

Adimora AA, Schoenbach VJ, Dohery IA. Concurrent sexual partnerships among men in the United States. Am J Public Health 2007; 97(12): 2230–2237.

Adimora AA, Schoenbach VJ, Taylor EM, Khan MR, Schwartz RJ. Concurrent partnerships, nonmonogamous partners, and substance use among women in the United States. Am J Public Health 2011; 101(1):128–136.

American College of Obstetricians and Gynecologists (ACOG). Addressing health risks of noncoital sexual activitiy. Committee Opinion No. 582. Obstet Gynecol 2013; 122:1378–1383.

Berkman ND, Sheridan SL, Donahue KE, Halpern DJ, Crotty K. Low health literacy associated with increased emergency department utilization and recidivism? Ann Intern Med. 2011;155(2):97–107.

Centers for Disease Control and Prevention. *Sexually Transmitted Disease Surveillance 2015*. Atlanta: U.S. Department of Health and Human Services; 2015. Available at https://www.cdc.gov/std/stats15/std-surveillance-2015-print.pdf

Centers for Disease Control and Prevention. Clinical advisory: Ocular syphilis in the United States. Updated March 34, 2016. Available at: https://www.cdc.gov/std/syphilis/clinicaladvisoryos2015.htm

Chandra A, Mosher WD, Copen C. Sexual behavior, sexual attraction, and sexual identity in the United States: Data from the 2006–2008 National Survey of Family Growth. National Health Statistics Reports, 2011; no. 36. Hyattsville, MD: National Center for Health Statistics.

Chen Y, McFarland W, Raymond HF, et al. Distribution of behavioral patterns before infection among San Francisco men who have sex with men newly infected with HIV in 2014. J Acquir Immune Defic Syndr 2017; 75(5): 528–534.

Chesson HW, Heffelfinger J, Voigt R, Collins D. Estimates of primary and secondary syphilis rates in persons with HIV in the United States, 2002. Sex Trans Dis 2005; 32(5):265–269.

Doshi M, Avery L, Kaddu RP, et al. Contextualizing willingness to participate: recommendations for engagement, recruitment & enrolment of Kenyan MSM in future HIV prevention trials. BMC Public Health 2017; 17:469.

Fortenberry JD, Orr DP, Zimet GD, Blythe MJ. Weekly and seasonal variation in sexual behaviors among adolescent women with sexually transmitted diseases. J Adolesc Health 1997; 20(6): 420-5.

Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. Sexually Transmitted Infections 1999; 75: 3–17.

Glynn TR, Operario D, Montgomery M, Almonte A, Chan PA. The duality of oral sex for men who have sex with men: an examination into the increase of sexually transmitted infections amid the age of HIV prevention. AIDS Patient Care and STDs 2017; 31(6): 261–267.

Gray RT, Hoare A, McCann PD, et al. Will changes in gay men's sexual behavior reduce syphilis rates? Sex Trans Dis 2011; 38(12):1151–1158.

Heckathorn D. Respondent-driven sampling: a new approach to the study of hidden populations. Social Problems 1997; 44(2): 174–199.

Heckathorn D. Respondent-driven sampling II: Deriving valid population estimates from chain-referral samples of hidden populations. Social Problems 2002; 49(1):11–34.

Jennings JM, Taylor RB, Salhi RA, Furr-Holden DM, Ellen JM. Neighborhood drug markets: A risk environment for bacterial sexually transmitted infections among urban youth. Social Science & Medicine 2012; 74:1240–1250.

Katz BP, Fortenberry JD, Tu W, Harezlak J, Orr DP. Sexual behavior among adolescent women at high risk for sexually transmitted infections. Sex Transm Dis 2001; 28(5): 247-51.

Kojima N, Davey DJ, Klausner JD. Pre-exposure prophylaxis for human immunodeficiency virus and sexually transmitted infection acquisition among men who have sex with men. AIDS 2016; (30):2251–2252.

Lindberg LD, Jones R, Santelli JS. Noncoital sexual activities among adolescents. Journal of Adolescent Health 2008; 43:231–238.

Lundborg P, Nilsson A, Rooth D. Parental education and offspring outcomes: evidence from the Swedish compulsory school reform. American Economic Journal; Applied Economics 2014; 6(1):253–278.

Melendez-Torres GJ, Hickson F, Weatherburn P, Bonell C. Nested event-level case-control study of drug use and sexual outcomes in multipartner encounters reported by men who have sex with men. AIDS and Behavior 2016; 20:646–654.

Morris M, Kretzschmar M. Concurrent partnerships and the spread of HIV. AIDS 1997; 11(5):641–648.

Pathela P, Hajat A, Schillinger J, Blank S, Sell R, Mostashari F. Discordance between sexual behavior and self-reported sexual identity: A population-based survey of New York City men. Annals of Internal Medicine. 2006; 145:416–425.

Paz-Bailey G, Mendoza M, Finlayson T, et al. Trends in condom use among men who have sex with men in the United States: the role of antiretroviral therapy and seroadaptive strategies. AIDS 2016; 30(12):1985–1990.

Purcell DW, Johnson CH, Lansky A, et al. Estimating the population size of men who have sex with men in the United States to obtain HIV and syphilis rates. The Open AIDS Journal 2012; 6, (Suppl 1: M6) 98–107.

Ramirez-Valles J, Heckathorn D, Vazquez R, Diaz RM, Carlson R. From networks to populations: The development and application of respondent-driven sampling among IDUs and Latino gay men. AIDS and Behavior 2005; 9(4):387–402.

Shettle C, Mooney G. Monetary incentives in U.S. government surveys. Journal of Official Statistics 1999; 15, 213–250.

Stoltey JE, Cohen SE. Syphilis transmission: a review of the current evidence. Sex Health 2015; 12(2):103–109.

Ulin P, Robinson E, and Tolley E. Qualitative methods in public health research. A Field Guide for Applied Research. 2005, San Francisco, CA: Jossey-Bass.

Volk JE, Marcus JL, Phengrasamy T, Blechinger D, Nguyen DP, Follansbee S, Hare CB. No new HIV infections with increasing use of HIV preexposure prophylaxis in a clinical practice setting. Clin Infect Dis 2015; 61:1601–1603.

Wang J, Carlson RG, Falck RS, et al. Respondent-driven sampling to recruit MDMA users: a methodological assessment. Drug and Alcohol Independence 2005; 78: 147–157.

Woolston S, Cohen SE, Fanfair RN, et al. Notes from the field: A cluster of ocular syphilis cases — Seattle, Washington, and San Francisco, California, 2014–2015. Morbidity and Mortality Weekly Report (MMWR) 2015; 64(40): 1150–1151. Available at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6440a6.htm

Yeka W, Maibani-Michie G, Prybylski D, Colby D. Application of respondent driven sampling to collect baseline data on FSWs and MSM for HIV risk reduction interventions in two urban centres in Papua New Guinea. Journal of Urban Health: Bulletin of the New York Academy of Medicine 2006; 83(7): i60–i72.

Zellner JA, Martinez-Donate AP, Sanudo F, et al. The interaction of sexual identity with sexual behavior and its influence on HIV risk among Latino men: Results of a community survey in Northern San Diego County, California. American Journal of Public Health. 2009; 99:125–132.