Network Epidemiology of Syphilis Transmission (NEST)

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Supporting Statement – Part B

Revision

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1. Respondent Universe and Sampling Methods

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. The size of the respondent universe for NEST is unknown. Men who have sex with men (MSM) are estimated to be 4% of the U.S. population (Purcell, 2012). But the number of MSM at high risk for syphilis either within the United States or within participating study cities is unknown, as such it is not possible to create sampling frames.

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. Study participants will be 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 sexual transmitted infections (STI) will be collected. These specimens include urine, blood, a pharyngeal swab, and a rectal swab. Data collected through 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 the sexual networks of MSM at increased risk of syphilis.

MSM will be recruited using respondent driven sampling (RDS). RDS is a chain-referral strategy in which a small number of men (“seeds”) are recruited into the study as participants and also serve as starting points for the chain-referral process. RDS has been found to be effective for recruiting populations that are “hidden” or difficult to reach and that are connected by strong social networks and ties. RDS is an established methodology utilized in a number of other federally funded surveillance projects, such as the National HIV Behavioral Surveillance (NHSB) study, Injecting Drug Users (IDU) and High-risk Heterosexuals (HET) at increased risk of infection cycles, (OMB No. 0920-0770, expiration date 3/31/2017). Previous studies using RDS have found that one-half to two-thirds of persons recruited by their peers for NHBS will present for eligibility screening

(Heckathorn, 2002; Ramirez-Valles, 2005; Wang, 2005; Yeka, 2006). Because recruiters are instructed to invite participation of their peers who meet the general eligibility criteria, it is expected that at least 90% of those presenting at the local study site for eligibility screening will be eligible (Ramirez-Valles, 2005). Study staff will recruit men into the study as the initial seeds. Seeds will complete all study activities as any other study participant. Each seed will then be asked to recruit a maximum of 6 individuals that they know and think meet the study eligibility criteria. Recruitment of other individuals for the study is voluntary. Participants who are enrolled into the study after having been referred will complete all study activities and will be asked to recruit others. This recruitment process continues until the target sample size has been reached. There may be variation in the specific RDS strategy employed at each site in order to reach the target population and the best methods for determining the criteria for selecting men as "seeds" and for identifying "seeds" will be determined locally by the sites. The final sample of 240 MSM per site will be generated from approximately 20 seeds. Across the study, target enrollment is a total of 720 enrolled participants (three study sites contributing 240 men from each site).

Sites applied to participate in NEST through a competitive application process. The target sample size for NEST will be approximately 240 MSM enrolled at each site (~ 720 MSM in total), where at least 10% of the sample will include MSM who have had a recent diagnosis of syphilis. Enrolled participants will need to meet the following inclusion criteria:

- have not previously participated in this syphilis research study,
- are at least 18 years of age,
- live in the participating MSA and plan to remain for the next 2 years,
- identify as male AND assigned male sex at birth (designated as male on original birth certificate),
- report having had sex (oral or anal sex) with a man in the past 6 months,
- had at least 1 sexual partner in the past 6 months,
- are able to provide contact and locator information for planned study visits,
- are lucid at time of consent and interview ("lucid" is defined as the ability to understand a basic description of the study and to meaningfully respond to interview questions).

An eligibility screening will be conducted by local study staff to assess whether potential participants meet these eligibility criteria.

2. Procedures for the Collection of Information

This will be a multi-site study enrolling a target sample of 720 MSM aged ≥ 18 years from three different geographic areas of the United States. The three geographic areas are: Chicago, Illinois; Baltimore, Maryland; and Columbus, Ohio. These men will need to provide consent and meet specific the inclusion criteria. The specific methods of contact and required consenting will be governed by each site's IRB requirements.

Study participation will include up to nine in-person visits i.e., a baseline visit and follow-up visits every 3-months thereafter for a total period of up to 24 months. At the baseline visit, study staff will provide a description of the study and administer a screening instrument to assess eligibility. If the respondent is deemed eligible, written consent will be obtained. All in-person visits will include completion of a survey (capturing demographics, sexual behaviors, healthcare access and utilization and other variables), enumeration of the participant's sexual network, and biological specimen collection for laboratory testing for syphilis, HIV, chlamydia, and gonorrhea. 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.

Four specimens (urine, blood, a rectal swab, and a pharyngeal swab) will be collected as part of this protocol at each visit. A portion of the blood sample will be used locally for screening for syphilis and HIV infection. A portion of the same blood sample will be sent to the CDC for confirmatory syphilis testing. If consent from the participant is obtained, an additional 10ml sample of blood will be collected and sent to CDC for storage and use for future sexual health research. The consent form includes a separate item of consent for blood sample storage/future use and clearly states that this is voluntary and that the participant is able to opt out of this storage/future use. The consent form also states that additional blood or blood products from each study visit will be used for future sexual health research. Any proposals for future use of these stored samples of blood will be reviewed by the CDC NEST study team to ensure that the intended use is in accordance with the language in the consent. The rectal and pharyngeal swabs and urine specimen will be used for testing for *N. gonorrhoeae* (gonorrhea) and *C. trachomatis* (chlamydia).

Information for NEST will be collected on one form (Attachment 3). Data elements collected on the NEST survey (Attachment 3) include participant demographics, sexual behavioral risk factors associated with STDs, detailed sexual network information, sex partner meeting places, healthcare access and utilization, social experiences that have been associated with increased risk of STIs among MSM (including experiences of stigma and discrimination), substance use (alcohol, injection and non-injection drug use),

participant knowledge and attitudes towards the use of HIV pre-exposure prophylaxis (PrEP), and STI laboratory test results. These data elements were developed collaboratively and agreed upon by members from all 3 participating NEST sites. Participant interview data will be maintained in electronic format by collaborating sites. Every third month, the local NEST site data manager will compile, clean, de-identify, recode, and transmit data to CDC through a secure access management system (SAMS). At CDC, data will be downloaded from SAMS, stored, and maintained by a data manager in the Surveillance and Data Management Branch, Division of STD Prevention, of the National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention.

CDC staff will routinely monitor completeness of reporting and the quality of data submitted. Site visits, regular communication with CDC, data quality checks and technical assistance will also provide opportunities for evaluation and troubleshooting of these processes. Data on race and ethnicity will be collected in compliance with the two-question format described in the 1997 Office of Management and Budget's standard for Maintaining, Collecting, and Presenting Federal Data on Race and Ethnicity, also known as Statistical Policy Directive 15.

3. Methods to Maximize Response Rates and Deal with No Response

Local sites have extensive prior research experience working with the target population and will use this experience to directly inform participant recruitment and retention. Specifically prior research findings will be used to: (1) describe the characteristics of local MSM; (2) gain an understanding of the context of syphilis risk behavior among MSM locally; (3) garner the support of community stakeholders; (4) identify MSM that could serve as seeds for recruitment; (5) identify venues attended by MSM; (6) assess the suitability of these venues for possible recruitment of participants and for data collection on venue affiliation; (7) develop questions of local interest for syphilis prevention among MSM; and (8) monitor the on-going implementation of the syphilis research study. Field staff who will recruit and interview enrolled participants will receive specialized training in contacting and interviewing MSM who are at high risk for syphilis. Recruitment will take place at sites affiliated with the three NEST awardees and will include local health departments, community LGBT organizations, local STD clinics and HIV/AIDS care facilities. Before starting any data collection activities, a short eligibility screener will be administered to prospective study participants. If the participant is deemed eligible consent will be obtained. Protocols for maximizing the likelihood of successful recruitment and interview with members of the target population will be developed and may vary by site. Similar study activities have been

conducted at the three NEST awardee sites and study staff have prior experience working with the target population.

4. Test of Procedures or Methods to Be Undertaken

Interview data
The NEST survey interview form was developed by the CDC. Survey questions were also based on input from previous CDC surveillance projects, including the National HIV Behavioral Surveillance (NHBS), and current research literature. Justification for the questions included in the NEST survey is provided in Attachment 3a.

Laboratory-based data
NEST will collect the results from local gonorrhea, chlamydia, syphilis, and HIV testing. These STI tests have all been validated by the local public health laboratories as required by relevant laboratory oversite authorities.

5. Individuals Consulted on Statistical Aspects and Individuals Collecting and /or Analyzing Data

CDC is not directly engaged with human subjects during data collection. However, CDC Project Staff below will train study site staff in data collection methods, monitor the progress of recruitment by health department staff, and analyze the data.

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Local data collection, management and analysis will be conducted at the three NEST sites, including:

1) The Ohio State University,
2) University of Illinois at Chicago, and
3) Baltimore City Health Department