Gonococcal Isolate Surveillance Project

OMB 0920-0307

Supporting Statement – Part A

REVISION

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Sancta St. Cyr
Project Officer

National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
Division of STD Prevention
Surveillance & Data Management Branch
Centers for Disease Control and Prevention
1600 Clifton Road NE, Mailstop E-63
Atlanta, GA 30329

Voice: (404)718-5447
Fax: (404)639-8610
Email: oew3@cdc.gov

GONOCOCCAL ISOLATE SURVEILLANCE PROJECT

0920-0307

Section A.

Justification.

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Section A. JUSTIFICATION

• Goal of the study: The Gonococcal Isolate Surveillance Project (GISP) was created to monitor trends in antimicrobial susceptibilities of *N. gonorrhoeae* in the United States. To increase capacity to detect and monitor resistant gonorrhea, this revision includes the collection of remnant nucleic acid amplification test (NAAT) samples and associated data elements along with an update to the data element choices for treatment received currently collected for all components of GISP.

• Intended use of the resulting data: Data from GISP are used to guide national gonorrhea treatment recommendations and monitor trends of antimicrobial resistant gonorrhea.

• Currently, data & specimens are collected at 30 participating sites where providers obtain urethral *N. gonorrhoeae* isolates from the first 25 men with urethral gonorrhea each month as part of core GISP activities. Under enhanced GISP (eGISP) activities, added to GISP in 2018, 10 of the 30 sites also collect 25 endocervical specimens from women, 25 extragenital specimens from men and women, and all isolates that are culture positive for *N. gonorrhoeae*, but negative by NAAT (suspected *Neisseria meningitidis*). A molecular surveillance activity under eGISP would allow 10 additional participating sites to submit gonorrhea-positive remnant NAAT specimens to CDC for molecular testing to characterize known gene mutations associated with gonococcal antimicrobial resistance.

• All GISP activities target the general population with presumed gonococcal infections.

• Data will be analyzed using trend analyses to identify changes in the burden of antibiotic resistance and cross-sectional analyses to identify risk factors for resistance.

1. Circumstances Making the Collection of Information Necessary

The Division of STD Prevention (DSTDP), National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP), Centers for Disease Control and Prevention (CDC) requests OMB to approve a revision to the currently approved version of 0920-0307, Gonococcal Isolate Surveillance Project (GISP) (expiration 8/31/2021). The purpose of this revision is to continue collection of surveillance data on antimicrobial resistance in *Neisseria gonorrhoeae* in the United States. These data are used by public health officials at the national, state, and local level to educate providers, allocate resources and implement local policies and procedures around gonorrhea.

This revision includes a new enhanced GISP activity to be performed at 10 participating sites to send remnant specimens from routine nucleic acid amplification testing (NAAT) to CDC for molecular evaluation of resistance-associated gonococcal gene mutations. Results of molecular resistance testing with associated data elements will improve the surveillance of antibiotic resistant gonorrhea by identifying resistance-associated gonococcal gene mutations in the absence of the need to perform bacterial culture. Additionally, this revision updates the data element choices for treatment received for all GISP surveillance activities as a result of the 2020 updated gonorrhea treatment recommendations. These changes allow GISP to both expand its ability to monitor gonococcal antimicrobial resistance independent of gonococcal cultures and to collect data reflective of the current recommended therapy for gonorrhea as part of surveillance. Requested changes to this ICR are further outlined in section 15 of this document and in **Attachment 9**.

Approximately 1.6 million new gonococcal infections occur annually in the United States.[1] Without treatment, gonorrhea can result in pelvic inflammatory disease, infertility, and ectopic pregnancy, and can also facilitate HIV transmission.[2] Gonorrhea control in the United States relies on prompt and effective antimicrobial therapy. However, treatment is complicated by the ability of *Neisseria gonorrhoeae* to develop antimicrobial resistance. Since its inception in 1986, GISP has been a unique national sentinel surveillance system that monitors trends in antimicrobial susceptibilities of *N. gonorrhoeae* in the United States and plays an integral role in guiding national treatment recommendations and national policy. The program and data collection are authorized by the Public Health Service Act, Sec. 301 and 318 (42 USC 241 and 247c) (**Attachment 1**).

In 2013 and again in 2019, *N. gonorrhoeae* was designated as an urgent antibiotic resistance threat in the United States by

CDC and remains a priority of the 2020 *National Plan for Combating Antibiotic-Resistant Bacteria*.[2-4] A fundamental component of the National Strategy is strengthening surveillance and this revision describes activities designed to strengthen surveillance of antimicrobial resistant *N. gonorrhoeae* to inform interventions and mitigate the spread of resistance.

Historically, healthcare providers at ~30 participating sentinel sites (i.e., STD clinic or multiple STD clinics affiliated with a single public health department) obtain urethral *N. gonorrhoeae* isolates from the first 25 men with symptomatic urethral gonorrhea each month. There may be occasional month-to-month variability in the number of isolates submitted; a sentinel site may provide >25 isolates in any given month to make up for providing <25 isolates in other months. The overall goal is for each site to provide at least 300 isolates per year. Isolates are shipped each month to a regional laboratory for antimicrobial susceptibility testing.

GISP has consistently provided robust data that allow monitoring of resistance trends and to inform updates to treatment guidelines. However, GISP core surveillance activities sample <4% of reported male gonorrhea cases in the United States and are limited to urethral infections only. In 2018, enhanced GISP (eGISP) began sampling female genital (endocervical and vaginal) and male and female extragenital (pharyngeal and rectal) anatomic sites, in addition to the male genital site already sampled in GISP core surveillance. Including isolates from the pharynx and other anatomic sites, as well as from women, expands on GISP's public health efforts to detect and respond to resistance more quickly. GISP surveillance was also strengthened with the addition of eGISP by identifying isolates that are culture positive for *N. gonorrhoeae,* but negative by NAAT, which is a more specific diagnostic test. This helped to ensure that non-gonococcal bacteria are excluded from gonococcal data, strengthening the accuracy and usefulness of GISP data, especially when clinical syndromes with other *Neisseria species* are indistinguishable from gonorrhea.

To further improve and strengthen GISP surveillance, this revision allows for a subset of sentinel sites (N=10) to conduct an additional enhanced surveillance activity in the form of molecular surveillance. Participating sites already locally performing NAATs would retain the leftover gonorrhea-positive samples (remnant) after diagnostic results have been determined and reported as part of standard care. The gonorrhea-positive remnant NAAT sample would be frozen, stored and then shipped directly to CDC on a monthly basis for molecular characterization of known resistance-conferring gene mutations. Remnant NAATs from

any anatomic site (including from the urethra, pharynx, rectum, vagina and cervix) of gonorrhea positive persons will be accepted. We anticipate up to ~70 positive remnant NAATs per month will be collected by each of these 10 sites.

To maintain accurate collection of GISP data elements, this revision also includes the updated weight-based dosing of ceftriaxone and cefixime. In December 2020, CDC released the Update to CDC's Treatment Guidelines for Gonococcal Infection. These new treatment recommendations increased the dose of the recommended regimen and the dose for an alternative regimen (ceftriaxone and cefixime, respectively).[5] These values, collected and recorded under the received treatment data element, are being added to allow for the collection of treatment data consistent with these updated recommendations.

Under this revision, there will be a change in annualized burden as 10 sentinel sites will be conducting maintenance and shipment of remnant NAAT specimens for molecular surveillance as part of enhanced GISP activities. There is not an increase in the number of data elements requested compared to what is collected for core or enhanced GISP activities. There is an overall increase in the burden of work for sites participating in molecular surveillance to maintain, freeze and then ship the remnant NAAT specimens to CDC.

Under this revision, the data collection and processes for all GISP activities are unchanged. The increased dosages for ceftriaxone and cefixime treatments allow for new data element options, but not a change in the number of data elements or the current work demand to collect them. All demographic/clinical data from the sentinel sites (**Attachment 3a1/ Attachment 3a2**) will be submitted electronically directly from the sentinel sites to the GISP data manager at CDC through (1) a secure data portal, or (2) through the CDC Secure Access Management Services partner portal and antimicrobial susceptibility testing results from the regional laboratories (**Attachment 3b1)** will be submitted electronically to the sentinel sites and to CDC through a secure data portal. To minimize burden, comma-separated values (csv) files that provide standardized structure of the electronic data are provided to sentinel sites and laboratories. Additionally, to further minimize burden, the regional laboratories will be able to extract electronic data directly from electronic laboratory information systems instead of hand entering data. Laboratories are also not required to report control strain testing results (**Attachment 3b2)**.

The GISP website (http://www.cdc.gov/std/gisp/) features information about GISP, program documents, and links to data reports. No data are collected on the website. The website does

not contain information about or pages directed at children under the age of thirteen years. This revision does not contain any changes to the GISP website.

2. Purpose of Use of the Information Collection

The purpose of GISP is to monitor trends in antimicrobial resistance in *N. gonorrhoeae* strains in the United States in order to establish a scientific basis for the selection of gonococcal therapies and to allow proactive changes to treatment guidelines before widespread resistance and failures of treatment occur. Overall GISP data are reported in the annual CDC STD Surveillance Report (https://www.cdc.gov/std/stats18/default.htm) and site-specific data are reported in the GISP Site Profiles (https://www.cdc.gov/std/stats18/gisp2018/default.htm).

CDC has designated *N. gonorrhoeae* as one of five "urgent" antibiotic resistance threats in the United States.[2] Responding to and monitoring antibiotic-resistant *N. gonorrhoeae* is a priority of the *National Plan for Combating Antibiotic Resistant Bacteria*.[3] This revision directly responds to the *National Strategy for Combating Antibiotic Resistant Bacteria* by improving and strengthening surveillance of gonococcal antimicrobial resistance through GISP. Additionally, data from GISP will also allow CDC to monitor and evaluate the effectiveness of public health interventions conducted to support the *National Strategy for Combating Antibiotic-Resistant Bacteria*.

GISP provides essential and unique data on gonococcal resistance patterns in the United States. Many non-GISP laboratories now use non culture-based tests (e.g., NAATs) to diagnose gonorrhea; without culture, the organism is not available for antimicrobial susceptibility testing. Thus, GISP fills critical surveillance needs. Also, adding molecular surveillance to GISP would expand antimicrobial resistance surveillance to areas unable to perform culture-based susceptibility testing. Without data from GISP, it would not be possible to know whether recommended antimicrobial therapies for gonorrhea remain effective over time. Without such information, both effective treatment and control of gonorrhea transmission would be jeopardized. By including data from molecular evaluation of remnant NAAT specimens, this revision will increase public health efforts to detect and respond to antimicrobial resistance more quickly.

Information from GISP is continually used as the basis for revising gonococcal treatment recommendations. GISP data have directly contributed to CDC STD Treatment Guidelines in 1989, 1993, 1998, 2002, 2004, 2006, 2007, 2010, 2012, 2015, and 2020, multiple recent reports, and the landmark CDC report, *Antibiotic*

Threats in the United States, 2013 and its updated version in 2019.[2,5-19] GISP data from 2005 to June 2006 indicated increased prevalence of fluoroquinolone-resistant *N. gonorrhoeae* (QRNG), which prompted CDC to no longer recommend empiric treatment for gonococcal infections with fluoroquinolones.[19,20] Several years later, data from GISP collected during 2006 to 2011 indicated increasing prevalence of isolates with elevated minimum inhibitory concentrations (MICs) of cefixime.[13,14] Based on these data, CDC updated treatment recommendations for gonococcal infections to no longer recommend cefixime as first-line therapy.[13] Based on the high prevalence of tetracycline resistance in GISP, CDC no longer recommended use of doxycycline (an antibiotic similar to tetracycline) as part of dual therapy for gonorrhea as of 2015.[6] In 2020, GISP provided data demonstrating the increasing trends of elevated MICs in azithromycin, which contributed to the removal of azithromycin as part of the recommended gonococcal treatment regimen.[5] Timely changes to treatment guidelines in response to subtle changes in resistance may help to stall or reverse the emergence of resistance, highlighting the importance of rapid identification of new resistance patterns and the role GISP plays in these efforts.

Despite the success of GISP over the last 30 years in effectively changing treatment guidelines to respond to the emergence of resistance, *N. gonorrhoeae* continues to develop new resistance patterns, as the number of new antibiotics continues to decline.[22] There is now only a single remaining recommended treatment regimen for gonorrhea[5] making surveillance of emerging resistance critical.

3. Use of Improved Information Technology and Burden Reduction

Under this revision, all demographic/clinical data from the participating sentinel sites (**Attachment 3a1/Attachment 3a2**) and antimicrobial susceptibility testing data (**Attachment 3b1**) from the regional laboratories will be submitted electronically either (1) directly from the sentinel site to the GISP data manager at CDC through a secure data portal, or (2) through the CDC Secure Access Management Services partner portal. All responses are gathered electronically. To minimize burden, comma-separated values (csv) files that provide a standardized structure of the electronic data are provided to sites (**Attachments 3a2 and 3b1).** Additionally, to further minimize burden, the regional laboratories will be able to extract electronic data from electronic laboratory information systems instead of hand entering data.

4. Efforts to Identify Duplication and Use of Similar Information

The principal investigators and co-investigators have completed a thorough review of the literature, and there is no similar surveillance system to monitor antimicrobial resistance in *N. gonorrhoeae* at the national level or regional level.

5. Impact on Small Business or Other Small Entities

Respondents include sentinel sites (STD clinical sites) and public health laboratories. 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 for collecting data/information and respondents are permitted to report data electronically to reduce burden and improve data quality. Respondents apply to participate in GISP and participate voluntarily.

6. Consequences of Collecting the Information Less Frequently

Past experience indicates that gonococcal resistance patterns can change rapidly. Therefore, the GISP protocol requests monthly reporting by sentinel sites in order to: (1) monitor emergence of new antimicrobial resistance or sudden changes in antimicrobial resistance trends, and (2) ease the burden of specimen processing for the participating laboratories. For these laboratories, it is easier to process isolates on an ongoing basis rather than store, process, and report them on a quarterly or annual basis.

After GISP detects an increase in suspected antimicrobial resistance patterns, appropriate responses (i.e., changes in guidelines, implementation of new therapeutic regimens, etc.) must be developed. With both culture-based and molecular surveillance specimen collection, there is the opportunity for quicker detection of new resistance, even more timely changes to treatment guidelines, and additional help to avert consequences of untreated gonorrhea, such as pelvic inflammatory disease and infertility. In addition, quicker detection of new resistance might allow public health responses to act quickly to contain the spread of resistant strains. There are no legal obstacles to reducing the burden.

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

This request fully complies with the regulation 5 CFR 1320.58.

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

A. A 60-day Federal Register notice was published in the *Federal Register* on March 8, 2021, Vol. 86, No. 43, pages 13394-13396 (**Attachment 2**). CDC received 0 comments (**Attachment 2a**).

B. GISP is a collaborative project among CDC investigators, regional laboratories, and 30 sentinel sites (STD clinics located around the United States). Frequent consultations between CDC and persons outside CDC regarding the availability of data, frequency of collection, clarity of instructions, and data elements to be recorded have taken place via: 1) site visits to participating sentinel sites and regional laboratories; 2) quarterly meetings of GISP co-investigators at the sentinel sites and regional laboratories; 3) e-mail communications among all personnel participating in GISP activities; 4) webinars for participating sentinel sites; and 5) informal discussions by phone held with nearly all participating sentinel sites about availability of data and barriers to data collection.

9. Explanation of Any Payment or Gift to Respondents

No payment or gift is provided to respondents.

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

The CDC Privacy Officer has assessed this package for applicability of 5 U.S.C. § 552a, and has determined that the Privacy Act applies to the information collected because there is a unique identifier assigned to the patient. This project will not collect name, social security number, or date of birth, but the Patient ID is a unique patient identifier assigned by the site that allows for linking of multiple isolates from a single person at a single clinic visit and across multiple clinic visits, and is provided to CDC for purposes of enhanced surveillance. The Patient ID number is used to facilitate communication between CDC and a reporting area when needed.

Sensitive information, such as gender of sex partners, HIV status, sex work exposure, and injection drug use are collected. The Patient ID serves as an identifier variable that will enable isolate and surveillance data to be linked back to patient identities at the local level, therefore personally identifiable information (PII) can be retrieved by an identifier assigned to an individual by a sentinel site.

At GISP core surveillance sites, isolates are collected from patients as part of their routine care when a gonorrhea infection is suspected. A unique number is assigned to each isolate. Isolates are assigned sequential identifiers for each month. Each identifier is composed of a three-letter designation for the STD clinic site, followed by a six-digit number indicating the year and month, and a two-digit number in the sequence from 01 through 25.

For the sites conducting enhanced GISP data and specimen collection activities (culture-based n=10; molecular n=10), additional data elements are collected, including a unique patient identifier that is assigned by the sentinel site. This identifier is created for the purposes of surveillance and is not a medical record number and does not include PII. Patient data are obtained through review of medical records by the clinic staff and include collection of demographic/clinical information. All PII is retained by the STD clinics that treated the patient and is not recorded with data sent to CDC or regional laboratories.

A current Privacy Impact Assessment (PIA) is included in this information collection request. The objective of the PIA is to systematically identify the risks and potential effects of collecting, maintaining, and disseminating personally identifiable information (PII) and to examine and evaluate alternative processes for handling that information to mitigate potential privacy risks and risks to confidentiality.

The electronic GISP database is stored on the CDC mainframe computer and only approved Division of STD Prevention (DSTDP) staff have access rights to the data.

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

IRB Approval

GISP activities have been determined to not involve research involving human subjects and IRB approval is not required (**Attachment 5a**).

Cases of gonorrhea are routinely reported to all state health departments, and patient information is routinely collected by state, county, and city health departments' STD program personnel for purposes of disease control. The clinical and demographic patient data collected for core and enhanced GISP activities (**Attachment 3a1/ Attachment 3a2, Attachment 7**) are a subset of this routinely collected information and information collected in the medical record.

Sensitive Questions

The sensitive questions in the demographic/clinical data include: Sex of sex partners, previous history of gonorrhea, HIV status, recent travel history, prior antimicrobial use, history of giving or receiving drugs or money for sex, and recreational drug use. (**Attachment 7**) These are elicited at participating STD clinics in a private environment and recorded by STD clinicians in order to assess behavioral and biological risk of infection, to guide appropriate behavioral counseling, and to determine the appropriate anatomic sites for STD testing or screening.[6] These questions are asked of all persons diagnosed with an STD and not specifically for GISP. These sensitive questions are essential to develop an accurate surveillance picture of disease in the community and to provide appropriate clinical care for each patient. These questions have been critically important for GISP in identifying epidemiological risk factors for antibiotic resistant gonorrhea. (**Attachment 8**)

Sex of sex partner and *recreational drug use* data help identify increased risk of gonorrhea – including transmission of resistant strains – in certain populations known to be at high risk for STDs. Men who have sex with men are at elevated risk for acquisition of resistant strains.[15,16,23]

Previous history of gonorrhea data are useful in determining whether antimicrobial resistance is more likely to emerge in core groups of individuals who have frequent gonococcal infections and are treated with antimicrobials frequently.[24-26]

HIV status data are useful for identifying increased transmission of resistant strains among certain immunosuppressed populations who may be engaging in risky sexual behavior. As data from GISP have demonstrated, HIV infection in some men might be a

marker of heightened risk for acquisition of resistant *N. gonorrhoeae* strains.[23]

Travel history, *prior antimicrobial use*, *history of giving or exchanging drugs or money for sex*, and *recreational drug use* have been associated with increased risk for infection with resistant gonorrhea and are risk factors associated with emergence of resistance.[23-26]

12. Estimated Annualized Burden Hours and Costs

Under this revision, there will be a change in burden as 10 sentinel sites will conduct molecular surveillance as part of GISP. These 10 sites will maintain, and ship to CDC already collected remnant NAAT specimens and submit accompanying clinical and demographic GISP data elements, increasing the total project burden.

For the 20 sentinel sites participating only in GISP core activities, clinics are asked to provide 25 isolates and associated demographic/clinical data per month. However, due to low volume at some sites in certain months, we expect an average of 20 isolate submissions per sentinel site per month for an estimated annual total of 240 isolates per sentinel site (20 isolates/month * 12 months). In total, from the sentinel sites participating only in core activities there will be an average of 400 isolate submissions per month (20 sentinel sites * 20 isolates/month) and average of 4,800 isolate submissions annually (400 isolates/month * 12 months).

For the 10 sentinel sites conducting enhanced culture-based activities and data collection in addition to the core activities, we expect an average of 70 isolate submissions per sentinel site per month for an estimated annual total of 840 isolates per sentinel site (70 isolates/month * 12 months). In total, from the sentinel sites participating in GISP culture-based enhanced and core activities, there will be an average of 700 isolate submissions per month (10 sentinel sites * 70 isolates/month) and average of 8,400 isolate submissions annually (700 isolates/month * 12 months).

Across the 30 sentinel sites participating in culture-based activities (20 conducting core activities only and 10 conducting core and enhanced activities), there will be an average of 1,100 isolate submissions per month (400 isolates from the 20 core sentinel sites + 700 isolates from the 10 enhanced sentinel sites) and average of 13,200 isolate submissions annually (1,100

isolates/month * 12 months).

All gonococcal isolates collected undergo antimicrobial susceptibility testing monthly by four regional laboratories. Each laboratory will test approximately 3,300 isolates annually (13,200 isolates per year / 4 labs) and in total, all four regional laboratories will test 275 isolates monthly (3,300 isolates / 12 months).

For the 10 sentinel sites conducting molecular-based enhanced surveillance, clinics are asked to provide up to 70 remnant NAAT specimens and associated demographic/clinical data per month. We expect half of clinics to provide an average of 20 male urethral only remnant NAAT specimens per sentinel site per month for an estimated annual total of 240 remnant NAAT specimens per sentinel site (20 remnant NAATs/month * 12 months) and the other half of clinics to provide an average of 70 male and female genital and extragenital remnant NAAT specimens per sentinel site per month for an estimated annual total of 840 remnant NAATs per sentinel site (70 remnant NAATs/month * 12 months). In total, from the sentinel sites participating in enhanced molecular surveillance activities, there will be an average of 450 remnant NAAT specimens submitted per month (5 sentinel sites * 20 remnant NAAT specimens/month + 5 sentinel sites * 70 remnant NAAT specimens/month) and average of 5,400 remnant NAAT submissions annually (450 remnant NAATs/month * 12 months).

All remnant NAATs retained and shipped to CDC will be tested monthly by CDC’s Laboratory Reference and Research Branch. The laboratory will test approximately 450 remnant NAATs per month and 5,400 annually.

For collection of demographic/clinical data and antimicrobial susceptibility data, a "response" is defined as the data collection/processing and laboratory processing associated with an individual isolate from an individual patient.

Each of the 20 sentinel sites that conduct core GISP activities will submit demographic/clinical data for the 20 isolates on a monthly basis or a total of 240 responses annually. (**Attachment 3a1**). The estimated time for clinic personnel to abstract these demographic/clinical data is 11 minutes per response. The estimated annual burden for these 20 sites is 880 hours per year.

Each of the 10 sentinel sites that will conduct culture-based enhanced GISP specimen and data collection in addition to core

activities will submit demographic/clinical data on approximately 70 isolates on a monthly basis or 840 responses annually. As four additional data elements are collected for these isolates, the estimated time for clinic personnel to abstract data for enhanced data collection is 12 minutes per response (**Attachment 3a2**) for a total annual burden across all sites of 1,680 hours.

Each of the 10 sentinel sites that will conduct molecular-based enhanced GISP with remnant NAATs will submit demographic/clinical data on up to 70 remnant NAATs on a monthly basis or up to 840 responses annually. As the data elements for these remnant NAAT samples are the same as collected for the culture-based surveillance, the estimated time for clinic personnel to abstract data for enhanced data collection is 12 minutes per response (**Attachment 3a2**) for a total annual burden across all sites of 1,680 hours.

On average, 1,100 isolates from culture are submitted monthly by the clinical sites for antimicrobial susceptibility testing; therefore, each of the four participating laboratories provides test results for approximately 275 isolates month or 3,300 isolates annually. Laboratories are able to extract data from electronic databases for submission to CDC to streamline data reporting. (**Attachment 3b1**) Combined with the estimated time for laboratories to conduct antimicrobial susceptibility testing, the total estimated time for each participating laboratory per response is 40 min. Total Annual burden is estimated as 8,800 hours annually.

Each of the 4 Regional laboratories tests 4 sets of 3 control strains each month or 12 sets of control strains annually (4 sets x 12 months = 48). It takes approximately 5 minutes to process one set of 3 control strains. (**Attachment 3b2**) The reporting of Control Strain Testing results is no longer required, but can be done at the same time of the reporting of the isolates susceptibility results. Total Annual burden for Control Strain Testing is estimated as 16 hours annually.

Thus, the estimated annualized burden across GISP is 13,056 hours.

Table A.12-1: 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
Sentinel site conducting culture-based core surveillance	Demographic/ Clinical Data (**Attachment 3a1**)	20	240	11/60	880
Sentinel site conducting culture-based enhanced surveillance	Demographic/ Clinical Data (**Attachment 3a2**)	10	840	12/60	1,680
Sentinel site conducting molecular enhanced surveillance	Demographic/ Clinical Data (**Attachment 3a2**)	10	840	12/60	1,680
Regional laboratory	Antimicrobial Susceptibility Testing Results (**Attachment 3b**)	4	3,300	40/60	8,800
	Control Strain Susceptibility Testing		48	5/60	16
Total		44			13,056

Use of the CDC GISP Secure Access Management Services partner portal or a secure data portal discussed in Item A.3 might reduce the burden required for clinic respondents when submitting demographic/clinical data. However, the time to record responses manually was used to calculate the burden.

Costs to respondents are incurred in purifying, storing and forwarding isolates to regional laboratories; storing and forwarding remnant NAAT specimens, transferring data from medical records to electronic GISP forms; entering the data into an electronic database locally (some clinics are currently not able to do this); and forwarding the information to CDC.

All respondents are paid through federal funds** so there is no additional cost to them to provide the isolates/data. However, in order to calculate the cost to the respondents, the average hourly wage rate for a clerk at the sentinel site (rates based on salary for Information and Record Clerk, All Other; $20.39/hour) and a lab technician (rates based on salary for Medical and Clinical Laboratory Technicians; $26.34/hour) from the U.S. Bureau of Labor Statistics May 2019 National Occupational Employment and Wage Estimates (available: https://www.bls.gov/oes/current/oes_stru.htm)

The total estimated annualized burden cost to respondents is $318,666.

Table A.12-2. Estimated Annualized Burden Costs

Type of Respondent	Form Name	No. of Respondents	No. of Responses per Respondent	Average Burden per Response (in hours)	Average Hourly Wage	Total Burden Cost
Sentinel site conducting culture-based core surveillance	Demographic/ Clinical Data (**Attachment 3a1**)	20	240	11/60	$20.39	$17,943
Sentinel site conducting culture-based enhanced surveillance	Demographic/ Clinical Data (**Attachment 3a2**)	10	840	12/60	$20.39	$34,255
Sentinel site conducting molecular enhanced surveillance	Demographic/ Clinical Data (**Attachment 3a2**)	10	840	12/60	$20.39	$34,255

Regional laboratory	Antimicrobial Susceptibility Testing Results (**Attachment 3b**)	4	3,300	40/60	$26.34	$231,792
	Control Strain Susceptibility Testing		48	5/60	$26.34	$421
Total		44				$318,666

** Respondents are paid through federal funds from the Epidemiology and Laboratory Capacity for Emerging Infectious Diseases (ELC) Cooperative Agreement.

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

The total annualized cost to the government is $1,286,900. The total cost to the government over the 3-year period is $3,860,700.

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)	$46,000
	CDC Laboratory Personnel (GS-15, .05 FTE)	$6,000
	CDC Laboratory Personnel (GS-13, .10 FTE)	$8,000
	CDC Laboratory Personnel (GS-12, .20 FTE)	$12,000
	CDC Laboratory Personnel (GS-11, .6 FTE)	$30,000
	CDC Laboratory Personnel (GS-9, .7 FTE)	$27,000
	CDC Epidemiologist (GS-15, .7 FTE)	$65,100

	CDC Project Coordinator (GS-11, .7 FTE)	$38,500
	Subtotal, Direct Costs to the Government	$232,600
Travel and other related expenses	Travel, supplies, and annual GISP report	$ 54,300
	Subtotal, Travel and other project-related expenses	$54,300
Federal Grant	Epidemiology Laboratory Capacity Grant	$ 1,000,000
	Subtotal, Federal Grant	$1,000,000
	TOTAL COST TO THE GOVERNMENT	$1,286,900

15. Explanation for Program Changes or Adjustments

The Gonococcal Isolate Surveillance Project (GISP) is the national surveillance system that monitors *Neisseria gonorrhoeae* antimicrobial susceptibility trends. Because *N. gonorrhoeae* resistance continues to emerge and fewer antimicrobial drugs are being brought to market, GISP is a critically important surveillance system. The project aims to continue to improve the way that surveillance is conducted. The current OMB approval expires on 8/31/2021.

This Revision involves a net increase in annualized burden, from 11,376 burden hours to 13,056 burden hours (+1,680). The number of sentinel sites (N=30) performing culture-based surveillance has not changed with the same amount of core surveillance sites (N=20) and sites that receive additional CDC funding to conduct enhanced surveillance (N=10). A new molecular-based activity involves sentinel sites (N=10) that are not required (but are encouraged) to participate in culture-based surveillance. There is no change in burden for the culture-based sentinel sites. The 10 sites participating in molecular-based enhanced surveillance activities will be subject to the annualized burden of this new activity. Estimates for each group are now provided in separate information collections. The changes in respondent burden are described in more detail below, along with the rationale for each

change and the measures taken to minimize burden, where applicable.

A. Molecular-based surveillance information collection at 10 sentinel sites

Ten (10) sentinel sites will conduct molecular-based enhanced surveillance which builds on the culture-based core and enhanced surveillance activities. Data collection for molecular-based surveillance consists of the same data elements and data collection tools as the culture-based enhanced surveillance activity.

1) New sample submission of remnant NAAT specimens to CDC for molecular characterization and evaluation

After NAATs were introduced in the 1990s as a more sensitive and specific method of diagnosing gonorrhea, the previous “gold standard” diagnostic test (gonococcal culture) has become less commonly used in clinics across the US. Culture retains the ability to perform susceptibility testing on isolates to identify known and emerging antimicrobial resistance. As the technology and knowledge has increased around the genetic mutations associated with antimicrobial resistance, extraction of genetic material from NAATs have led to the identification of resistance in the absence of a viable gonococcal culture. Molecular surveillance allows GISP to expand antimicrobial resistance surveillance in clinics and areas of the US that have been unable to previously monitor resistance by collecting the leftover NAAT samples already collected for routine care and identifying mutations in known resistance-conferring genes. Each molecular surveillance sentinel site will submit up to 70 remnant NAAT samples per month. Therefore, each site participating in molecular surveillance will submit an average of 840 remnant NAATs per year (70 isolates per month x 12 months). Expanding GISP in this manner is expected to allow public health officials to detect and respond to resistance more quickly, especially in areas without any antimicrobial surveillance being conducted.

2) Clinical and demographic data elements

All data elements being collected for culture-based enhance surveillance are the same data elements that will be collected for molecular surveillance. These data elements are already included in the clinical and demographic reporting requirements for enhanced surveillance (**Attachment 3a2**). The estimated burden per response is the same for molecular surveillance as it is for culture-based enhanced surveillance: 12 minutes.

The total estimated annualized burden for molecular surveillance is 1,680 hours (10 sentinel sites x 840 remnant NAATs per site x 12 minutes per response). Of this total, 440 hours would have been incurred if the 10 sites had continued participating at the core surveillance level, 40 hours would be needed to upgrade the clinical and demographic data elements at the core level of participation (240 isolates per year), and 1,200 hours are attributable to increasing the number of isolates per year (N=600) and submitting enhanced clinical and demographic information on these isolates.

Summary of Changes that Affect Sentinel Sites

	Type of Respondent	Type of data elements	Number of Respondents	Number of responses per respondent	Average burden per response	Total burden hours
Previous approval	Core surveillance sites	Core clinical and demo-graphic data elements (**Attach-ment 3a1**)	20	240	11/60	880

	Enhanced surveillance sites	Enhanced clinical and demographic data elements (**Attachment 3a2**)	10	600	12/60	1,200
Revision request	Core surveillance sites (culture-based surveillance)	Core clinical and demographic data elements (**Attachment 3a1**)	20	240	11/60	880
	Enhanced surveillance sites (culture-based surveillance)	Enhanced clinical and demographic data elements (**Attachment 3a2**)	10	600	12/60	1,200
	Enhanced surveillance sites (molecular surveillance)	Enhanced clinical and demographic data elements (**Attachment 3a2**)	10	600	12/60	1,200

16. Plans for Tabulation and Publication and Project Time Schedule

Table A.16: Project Time Schedule

Activity	Time Schedule
Collection of isolates, remnant NAAT specimens, and clinical/demographic data from sentinel sites (STD clinics)	August 2021
Processing and testing of isolates at regional labs	Monthly after OMB approval
Download data from secure file transport from sentinel sites and laboratories to CDC	Monthly after OMB approval
Data management and validation of data collected	Quarterly after OMB approval
Dissemination of results via annual report	12 months after OMB approval and annually

Preliminary data analysis is expected to begin 4 – 6 months after OMB approval and final analysis of the first year of data collection is expected to be completed 12 months after OMB approval. Additional data analysis will occur at least annually during the time period of the approved 3-year extension. Data analyses include descriptive analyses and trends in gonococcal antimicrobial resistance over time. Trends are presented as a percentage of isolates which are resistant to specific antimicrobial agents. Summary tables of demographic/clinical characteristics by antimicrobial resistance patterns are generated. Summary reports of GISP data are included in annual STD surveillance reports published by CDC (available at http://www.cdc.gov/std/). Site-specific GISP data are published on-line annually (Available at http://www.cdc.gov/std/gisp/). In addition, analyses of the data are published in scientific and public health journals and presented at scientific meetings. The information from these reports of the GISP data are often used by CDC, state and local STD program managers for program planning and resource allocation; non-STD program policy makers; clinical and laboratory researchers; and others.

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.

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