The GAIN (Greater Access and Impact with NAT) Study: Improving HIV Diagnosis, Linkage to Care, and Prevention Services with HIV Point-of-Care Nucleic Acid Tests (NATs)

New

SUPPORTING STATEMENT A

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• **Goal of the study**: GAIN is an implementation study to compare a point-of-care nucleic acid HIV test (HIV RNA POC NAT) to standard lab-based HIV testing. Aims of the project include: 1. Evaluate impact of HIV RNA POC NAT on pre-exposure prophylaxis (PrEP)-related clinical outcomes, 2. Evaluate impact of HIV RNA POC NAT on HIV clinical care outcomes, 3. Evaluate impact of HIV RNA POC NAT on time to virologic suppression, 4. To quantify acceptability and feasibility of POC NAT and collect cost and related data, and 5. To compare sensitivity and specificity of multiple POC NATs over a range of HIV RNA levels.

• **Intended use of the resulting data**: These data will be analyzed and disseminated to describe the real-world performance and clinical effects of HIV RNA POC NAT testing technology. This study will develop functional models to integrate HIV RNA POC NAT testing technology into HIV prevention and treatment services.

• **Methods**: Study activities include: 1. Retrospective baseline data collection from clinical site electronic medical records. This will establish baseline PrEP and HIV care metrics for comparison after study implementation; 2. A longitudinal, prospective study of HIV-negative patients seeking HIV testing and/or PrEP services; 3. A longitudinal, prospective study of HIV-positive patients seeking STI testing; 4. An RCT of POC NAT or Standard of Care for HIV-positive patients; 5. A survey, interviews, and focus groups examining POC NAT acceptability among HIV-negative and HIV-positive patients; 6. A cross-sectional comparison of several point-of-care NATs among HIV-positive patients; 7. Acceptability/feasibility assessment among clinical and community providers and costing analyses.

• **Subpopulation**: The target populations for this study are persons at high-risk for acquiring HIV infection and HIV-positive persons who are not virally suppressed, including those who are newly identified and those who are out of care.

• **How data will be analyzed**: Specific analyses to address each of the five study aims will be conducted using appropriate statistical software (i.e. SAS), using data from electronic health records, study visit records, laboratory results, and participant and provider surveys, interviews, and focus groups. Only de-identified data will be transmitted to CDC.

• **Impact of Covid-19 Pandemic:** This information collection is not impacted by the pandemic. All study activities will be conducted in line with the University of Washington's COVID-19 prevention policies (https://www.washington.edu/research/announcements/mitigating-impacts-to-research-activities-due-to-covid-19/#field).

1. Circumstances Making the Collection of Information Necessary

The Centers for Disease Control and Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP), Division of HIV/AIDS Prevention (DHAP) requests a 3-year approval for a new data collection called "The GAIN (Greater Access and Impact with NAT) Study: Improving HIV Diagnosis, Linkage to Care, and Prevention Services with HIV Point-of-Care Nucleic Acid Tests (NATs)."

In 2016, HIV infection was diagnosed in 39,782 people in the United States. Black/African American (26%) and Hispanic/Latino gay, bisexual, and other men who have sex with men (MSM) (18%) were among the most affected groups.[1] Pre-exposure prophylaxis (PrEP) can prevent HIV acquisition among persons at risk.[2] To prevent the emergence of drug-resistant HIV strains, prior to initiating PrEP, persons must be tested for HIV to ensure that they are not infected. Current rapid point-of-care (POC) technologies do not reliably detect the earliest HIV infections and lab-based testing can introduce delays while patients wait for test results. During this time, patients can drop out of care and are still at high-risk to become HIV infected. Direct molecular detection of HIV through nucleic acid tests (NATs) can identify early HIV infections, which have high potential for transmission. NATs that are used at the point-of-care (POC NAT) can provide results in 60 to 90 minutes. Obtaining timely molecular test

[1] Centers for Disease Control and Prevention. HIV Surveillance Report: Diagnoses of HIV Infection in the United States and Dependent Areas, 2016. Volume 28. Available from: http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html

[2] Centers for Disease Control and Prevention. US Public Health Service: Pre-exposure prophylaxis for the prevention of HIV infection in the United States—2017 Update: a clinical practice guideline 2018. Available from: https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

results from a POC NAT in clinics or community settings can expand prevention as well as HIV treatment services, improve our reach into disproportionately affected populations, and provide opportunities to approach the goal of no new HIV infections.[3-4]

In 2015, the U.S. Food and Drug Administration (FDA) first approved and granted Clinical Laboratory Improvement Amendments (CLIA) waivers for multiple POC NATs to diagnose influenza, streptococcus, and RSV infections. Devices used to perform these POC NATs can also be used to detect HIV-1 nucleic acid. Outside of the U.S., several POC NAT platforms are approved for HIV diagnosis and quantification. However, in the United States (U.S.), available POC testing with FDA-approved tests can only detect HIV p24 antigen and antibodies, which are only measurable days to weeks after nucleic acid detection. In the future, it is anticipated that the FDA will approve HIV POC NATs to diagnose and monitor HIV infections in the U.S.; until then, these tests can be used in a research capacity in community and clinical settings.

In PrEP clinics, systematic use of an HIV POC NAT to test at-risk persons, regardless of whether they have symptoms of acute HIV infection or not, would facilitate the identification of uninfected individuals who would benefit from initiating PrEP within a single care visit. To expedite PrEP initiation, rapid creatinine tests could also be implemented to assess renal function (a recommended safety

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[3] Skarbinski J, Rosenberg E, Paz-Bailey G, Hall HI, Rose CE, Viall AH, et al. Human immunodeficiency virus transmission at each step of the care continuum in the United States. JAMA Internal Medicine. 2015;175(4):588-96.

[4] Gopalappa C, Farnham PG, Chen YH, Sansom SL. Progression and Transmission of HIV/AIDS (PATH 2.0). Med Decis Making. 2017;37(2):224-33.

test). HIV POC NATs could also facilitate more expedient treatment for persons diagnosed with an HIV infection.

Community-based settings can reach populations at disproportionate risk for HIV, such as black/African American and Hispanic/Latino MSM, who may not regularly access HIV testing in clinical settings. The use of HIV POC NATs may reduce the time between testing and PrEP initiation among persons at high risk, and may reduce the time between testing and treatment initiation or re-engagement for those who are diagnosed with HIV. Further, an HIV POC NAT to detect viral load at the time of diagnosis may provide information on the risk of progression of disease, and for transmission to sex and drug-sharing partners, that might improve motivation to link to HIV treatment.

The purpose of this research is to develop feasible and effective models for using HIV POC NATs to: (1) improve PrEP initiation, and duration of PrEP use, among persons at high-risk for acquiring HIV infection; and (2) reduce the time between testing in community-based and clinical-based settings and linkage to HIV care, ART initiation, and viral suppression.

CDC requests OMB approval to collect the information needed to understand the real-world performance of these laboratory tests and the models to implement them into practice. OMB approval is requested for 3 years. CDC is authorized to conduct the information collection under Section 306 of the public Health Services Act [42 U.S.C.A.2. (**Att. 1**).”

2. Purpose and Use of the Information Collection

The purpose of the research is to develop feasible and effective models for using HIV point-of-care (POC) nucleic acid tests (NATs) to improve HIV prevention services and HIV care outcomes. The University of Washington (UW) will conduct the study, with consultation and technical expertise from CDC. The study sites will be clinics providing HIV and sexually-transmitted infection (STI)testing and treatment. Study objectives include: 1. Evaluate impact of HIV RNA POC NAT on PrEP-related clinical outcomes, 2. Evaluate impact of HIV RNA POC NAT on HIV clinical care outcomes, 3. Evaluate impact of HIV RNA POC NAT on time to virologic suppression, 4. To quantify acceptability and feasibility of POC NAT and collect cost and related data, and 5. To compare sensitivity and specificity of multiple POC NATs over a range of HIV RNA levels. The study will take place at two clinics in Seattle. Activities include: 1. Retrospective baseline data collection from clinical site electronic medical records (EHRs), 2. A longitudinal, prospective study of HIV-negative patients seeking HIV testing and/or PrEP services, 3. A longitudinal, prospective study of HIV-positive patients seeking STI testing, 4. An RCT of POC NAT or Standard of Care for HIV-positive patients at Madison Clinic, 5. A survey, interviews, and focus groups examining POC NAT acceptability among HIV-negative and HIV-positive patients, 6. A cross-sectional comparison of several point-of-care NATs among HIV-positive patients,

7. Acceptability/feasibility assessment among clinical and community providers and costing analyses.

Study activities to address these objectives are outlined in the GAIN study activities and visual overview (**Att. 3**). The specific data collected and specimen types are detailed in the GAIN data sources and variables table (**Att. 4**).

3. Use of Improved Information Technology and Burden Reduction

UW will utilize EHR data to efficiently establish baseline HIV prevention and care metrics for study comparisons. UW has identified and will use clinical databases (e.g. INSYNC database (https://www.insynchq.com/privacy, UWHIS database) to extract necessary study data without the need for additional collection (**Att. 4**). All data will be transmitted to CDC electronically using a Secure File Transfer Protocol (FTP).

4. Efforts to Identify Duplication and Use of Similar Information

Due diligence was applied to identify duplication of study objectives and planned data collection. As detailed in section 1. Circumstances Making Collection of Information Necessary, HIV POC Nat tests are not yet approved by the FDA for clinical use outside of a research capacity in community and clinical settings. The need for these data drove the development of the study objectives. UW is not collecting these data for other purposes prior to study initiation, the data will be collected to address the study's unique objectives.

5. Impact on Small Business or Other Small Entities

No small businesses will be involved in this study.

6. Consequences of Collecting the Information Less Frequently

UW will submit a monthly study report form to CDC (**Att. 5. GAIN monthly study report form**). UW will send cumulative de-identified study datasets to CDC on a semiannual basis. Less frequent data submission could result in a lag time between the occurrence of study problems and their identification. This lag time could result in costly inefficiencies, defects, and failures to improve without a timely opportunity for CDC to provide valuable assistance and corrective measures. The planned reporting framework balances UW's reporting burden and CDC's need to need to monitor and support study activities.

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

This request fully complies with the guidelines of 5 CFR 1320.5.

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

A 60-day Federal Register notice to solicit public comments was published on 12/21/2020, Volume 85, Number 245, Pages 83087-83089 (**Att. 2**). Two public comments were received (Att. 2A). Neither commenter provided contact information so no CDC comments were sent.

9. Explanation of Any Payment or Gift to Respondents

Tokens of appreciation of a value ≤$20 will be provided to participants in the randomized controlled trial, multi-NAT group, survey group, and provider group. Participants in the interviews or focus groups will receive a token of appreciation ≤$40. These tokens of appreciation support study participation and their use has been approved by the University of Washington Institutional Research Board (IRB) (**Att. 6**). Similar tokens of appreciation have been demonstrated to increase study participation, as in the National Survey on Drug Use and Health, conducted by the Substance Abuse and Mental Health Services Administration (SAMHSA), where participants receiving no token of appreciation had a participation rate of 69%, compared to 79% among those receiving $20, and 83% among those who receiving $40 (OMB No. 0930-0110, exp. 10/31/2022).[5] Additionally, a randomized controlled trial demonstrated that offering nominal tokens of appreciation (<$50) to persons recruited to complete online surveys yielded greater response rates and decreases response time compared to no tokens of appreciation.[6]

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

[5] J. Kennet, J. Groerer, K.R. Bowman, et al. Evaluating and improving methods used in the National Survey on Drug Use and Health. Substance Abuse and Mental Health Services Administration, Rockville (MD). 2005. https://books.google.com/books?hl=en&lr=&id=phs7YtaK3zcC&oi=fnd&pg=PA1&ots=DZ9MWKBJQp&sig=BVjJ7wXEJYSGPvt5Vb1es3GQ_as#v=onepage&q&f=false

[6] Turnbull AE, O'Connor CL, Lau B, Halpern SD and Needham DM. (2015). Allowing physicians to choose the value of compensation for participation in a web-based survey: randomized controlled trial. J Med Internet Res 17, 7: 1-10

The CDC/ATSDR Privacy Officer, has assessed this package for applicability of 5 U.S.C. § 552a, and determined that the Privacy Act applies/does not apply to the overall information collection (**Att. 7**).

Documents containing identifiers will be handled only by trained study staff and will be stored securely. All digital participant information will be maintained in a secure, password-protected electronic form to which only study staff and relevant auditors (e.g. UW Human Subjects Division) will have access. The CDC will receive only de-identified data (**Att. 4)** Although the instrument collects PII such as name, date of birth (DOB), phone number, email address, , study ID, EMR ID, and blood specimens (plasma and cell pellet specimens from blood draw for POC NAT test) these data are collected and retained by UW. These data are necessary for UW to conduct the study, including matching patient sample to lab results, notifying patients of lab results by phone (if necessary, most results will be communicated at the clinical visit, however, if a patient has to leave before results are available the study staff must have a way to contact the patient with results), and emailing links to a feedback survey if patients agree to participate. UW procedures for handling PII in this study are IRB approved. No PII will be sent to CDC. All existing links between identifiers and data will be destroyed six years after study completion.

Participants will be fully advised about the privacy and security of their information, including limitations to confidentiality, prior to study participation. These protections and limitations are outlined in

the “Confidentiality of Research Information” sections of the IRB-approved consent forms (**Att. 8.** Consent form: GAIN Study – Testing, PEP & PrEP Group; **Att. 9.** Consent form: GAIN Study – Gay City HIV+ Group; and **Att. 10.** Consent form: GAIN Study – RCT Group).

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

IRB Approval

The University of Washington IRB has approved the study as outlined in the attached IRB approval letter (**Att. 6**).

Sensitive Questions

HIV can be transmitted through sexual contact and the sharing of HIV contaminated needles and syringes. Questions that relate to individual behavior and modes of transmission may be sensitive for some individuals. However, collection of such information is important to assessing the real-world use and impact of POC HIV NAT tests and implementation programs related to these tests. Concerns about sensitive questions are most relevant to the survey group as the survey will include questions about sexual behavior and injection drug use. Persons approached about study participation will be advised about these concerns prior to providing consent (**Att. 8.** Consent form: GAIN Study – Testing, PEP & PrEP Group; **Att. 9.** Consent form: GAIN Study – Gay City HIV+ Group). They will also be advised to take the

survey in a private location, and they will be informed about the confidentiality of their responses.

12. Estimates of Annualized Burden Hours and Costs

The burden estimate is based on the University of Washington conducting the study at two clinical locations. Study participants are persons seeking medical care at Gay City Clinic and Madison Clinic who consent to study participation. The study includes seven activities. It is possible that a single individual could be a participant in more than one study activity (e.g. a participant in the prospective study of HIV-negative patients may participant in the survey group). However, in these estimates, we treat the number of study participants/respondents in each study activity as distinct persons as it is not possible to estimate the exact degree of overlap. Each study activity and a description of how it is considered in the estimates of annualized burden hours is included in the numbered list below. Annual study enrollment is estimated from the total enrollment divided over 3 years.. **Att. 11** is the IRB-approved GAIN study visit survey that will be completed by participants in the prospective studies, RCT, and cross-sectional comparison. **Att. 12** is the IRB-approved survey that will be completed by participants in the survey group examining POC NAT acceptability. **Att. 13** includes the IRB-approved focus group and interview guides for the acceptability/feasibility assessment among clinical and community providers. As the focus group and interviews will be conducted by a guide/interviewer and are not computer-based, no screenshots are indicated. **Att. 14** is the GAIN ROI form, **Att. 15** is

the Baseline data collection variables list, and **Att. 16** is the GAIN patient information sheet (verbal consent completed by participants in the cross-sectional comparison group).

1. Retrospective baseline data collection: these data will be abstracted from existing clinic EHR systems by UW study staff.. In the burden tables (**Exhibit A.12-A,B)**the respondents for this activity are the data managers at each study site who will abstract these data and submit the aggregate, deidentified data reports. (
2. Prospective study of HIV-negative patients seeking HIV testing and/or PrEP services: this activity will enroll a maximum of 4600 study participants, estimated annual enrollment: 1150
3. Prospective study of HIV-positive patients seeking STI testing: this activity will enroll a maximum of 500 study participants, estimated annual enrollment: 125.
4. RCT of POC NAT or Standard of Care for HIV-positive patients: this activity will enroll a maximum of 1000 study participants, estimated annual enrollment: 250.
5. Survey group examining POC NAT acceptability among HIV-negative and HIV-positive patients: this activity will enroll a maximum of 350 study participants, estimated annual enrollment: 87.
6. Cross-sectional comparison of several point-of-care NATs among HIV-positive patients: this activity will enroll a maximum of 1000 study participants, estimated annual enrollment: 250.

7. Acceptability/feasibility assessment among clinical and community providers: this activity will enroll a maximum of 100 study participants, estimated annual enrollment: 25. Participants may complete a survey, interview, or focus group. Time for completion will vary between these activities, the largest amount of time (1 hr) is included in the table. In the burden tables (**Exhibit A.12-A,B)** the respondents for this activity are healthcare providers.

Exhibit A.12-A. Estimated Annualized Burden Hours

Type of Respondent	Form Name	Number of Respondents	Number of Responses per Respondent	Average Burden per Response (in Hours)	Total Burden (in Hours)
Participating Clinic	Baseline data collection variables list	2	1	2	4
	Monthly study report form	2	12	15/60	6
Participants in prospective study of HIV-negative patients seeking HIV testing and/or PrEP services	Release of information form	1530	1	10/60	255
	Study visit survey	1530	1	15/60	383
Participants in prospective study of HIV-positive patients seeking STI testing	Release of information form	165	1	10/60	28
	Study visit survey	165	1	15/60	41
Participants in RCT of POC NAT or Standard of Care for HIV-positive	Release of information form	333	1	10/60	56
	Study visit survey	333	1	15/60	83

patients					
Participants in survey group examining POC NAT acceptability	POC NAT acceptability survey	117	1	20/60	39
Participants in cross-sectional comparison of several point-of-care NATs	Release of information form	333	1	10/60	56
	Study visit survey	333	1	15/60	83
Acceptability/ feasibility assessment among clinical and community providers	POC NAT acceptability survey, focus group, or interview	33	1	1	33
Total					1,067

B. Annualized Cost to Respondent

The hourly wage rate used for the data managers (activity 1. Baseline data collection) and for study participants (activities 2-6) is the median hourly wage for all occupations in the May 2019 National Occupational Employment and Wage Estimates provided by the U.S. Bureau of Labor Statistics (https://www.bls.gov/oes/current/oes_nat.htm#00-0000). The hourly wage rate used for the provider survey group (activity 7) is the median hourly wage for the healthcare practitioners and technical occupations category in the May 2019 National Occupational Employment and Wage Estimates provided by the U.S. Bureau of Labor Statistics (https://www.bls.gov/oes/current/oes_nat.htm#29-0000).

Exhibit A.12-B. Annualized Cost to Respondents

Type of Respondent	Form Name	Total Burden	Hourly Wage	Total Respondent

		(in Hours)	Rate	Cost
Participating clinic	Baseline data collection variables list	4	$19.14	$77
	Monthly study report form	6	$19.14	$115
Participants in prospective study of HIV-negative patients seeking HIV testing and/or PrEP services	Release of information form	255	$19.14	$4881
	Study visit survey	383	$19.14	$7331
Participants in prospective study of HIV-positive patients seeking STI testing	Release of information form	28	$19.14	$536
	Study visit survey	41	$19.14	$785
Participants in RCT of POC NAT or Standard of Care for HIV-positive patients	Release of information form	56	$19.14	$1072
	Study visit survey	83	$19.14	$1589
Participants in survey group examining POC NAT acceptability	POC NAT acceptability survey	39	$19.14	$746
Participants in cross-sectional comparison of several point-of-care NATs	Release of information form	56	$19.14	$1072
	Study visit survey	83	$19.14	$1589
Acceptability/feasibility assessment among clinical and community providers	POC NAT acceptability survey, focus group, or interview	33	$32.78	$1082
Total		1,067		$20,873

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

There are no other costs to respondents or record keepers associated with this study.

14. Annualized Cost to the Federal Government

The annualized cost to the government is $1,346,479. Costs to the federal government include federal employee time allocated for technical assistance, collaboration, and data management on this project. Technical assistance and collaboration will occur through email, phone calls, and annual site visits. Over the course of the project various CDC staff will collaborate and contribute to this research. It is estimated that annually the equivalent of two GS-13 step 9 ($58.34/hour) FTEs will expend approximately twenty-five percent (25%) of working hours (1040 hours) contributing to this project.

Managing and analyzing data reported to CDC from this project is projected to require the expertise of the equivalent of two data managers and two data analysts. The data managers would be at the pay scale of GS-13 step 5 ($52.20/hour) and the data analysts would be at the pay scale of GS-12 step 5 ($43.90/hour).

Exhibit 14.A Annualized Cost to the Government

Cost	**Annual Burden (in hours)**	**Hourly Wage Rate**	**Annual Cost**
Cooperative agreement costs	Not applicable	Not applicable	$890,189
Federal employee time: Technical assistance and collaboration	1,040	$58.34	$60,674
Federal employee time: Data monitoring and	4,160 (Data Managers)	$52.20	$217,152

analyzing	4,160 (Data Analysts)	$42.90	$178,464
TOTAL ANNUAL FEDERAL GOVERNMENT COSTS:		$1,346,479	

Source: **http://www.opm.gov/policy-data-oversight/pay-leave/salaries-wages/salary-tables/pdf/2020/ATL.pdf**

15. Explanation for Program Changes or Adjustments

This is a new information collection request.

16. Plans for Tabulation and Publication and Project Time Schedule

Data collection will be conducted during the 3-year period after OMB approval. GAIN study data will be submitted to CDC on a semiannual basis. Data analysis will occur within 12 months of final data collection. The following is a brief overview of the anticipated study timetable:

Activity	Time Schedule
Begin study participant enrollment at clinical sites	Immediately after OMB approval
First semi-annual reporting of GAIN data	.5 years after OMB approval
Second semi-annual reporting of GAIN data	1 years after OMB approval
Third semi-annual reporting of GAIN data	1.5 years after OMB approval
Fourth semi-annual reporting of GAIN data	2 years after OMB approval
Fifth semi-annual reporting of GAIN data	2.5 years after OMB approval
Sixth semi-annual reporting of GAIN data	3 years after OMB approval

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

CDC is not seeking approval to not display the expiration date.

18. Exceptions to Certification for Paperwork Reduction Act (PRA) Submissions 5CFR 1320.3(h)(1)-(10)

There are no exceptions to the certification.